PRV

PATENT- OCH REGISTRERINGSVERKET
Patentavdelningen

Intyg
Certificate

Härmed intygas att bifogade kopior överensstämmer med de handlingar som ursprungligen ingivits till Patent- och registreringsverket i nedannämnda ansökan.

This is to certify that the annexed is a true copy of the documents as originally filed with the Patent- and Registration Office in connection with the following patent application.

(71) *Sökande* *Biolipox AB, Stockholm SE*
Applicant (s)

(21) *Patentansökningsnummer* *0302035-1*
Patent application number

(86) *Ingivningsdatum* *2003-07-09*
Date of filing

Stockholm, 2004-02-10

För Patent- och registreringsverket
For the Patent- and Registration Office

Hjördis Segerlund

Avgift
Fee *170:-*

PATENT- OCH REGISTRERINGSVERKET
SWEDEN

Postadress/Adress
Box 5055
S-102 42 STOCKHOLM

Telefon/Phone
+46 8 782 25 00
Vx 08-782 25 00

Telex
17978
PATOREG S

Telefax
+46 8 666 02 86
08-666 02 86

NEW COMPOUNDS

FIELD OF THE INVENTION

This invention relates to novel compounds, to pharmaceutical compositions comprising the compounds, as well as to the use of the compounds in medicine and for the preparation of a medicament, which acts on the membrane associated prostaglandin E_2 synthase (mPGES) enzyme. It is of special interest to provide a treatment or alleviation of inflammatory diseases and disorders having an inflammatory component, for the treatment or alleviation of pain, and for the alleviation of fever.

BACKGROUND OF THE INVENTION

Arachidonic acid is converted by the cyclo-oxygenase (COX) to the unstable intermediate prostaglandin (PG) H_2, which is further metabolized to other prostaglandins (e.g. PGE_2, $PGF_{2\alpha}$, PGD_2 etc), prostacyclin and thromboxane. These metabolites are highly potent compounds, with both physiological and pathophysiological effects. The COX enzyme exists in two forms, one which is constitutively expressed in many cells and tissues (COX-1) and one form, which is induced by proinflammatory cytokines during an inflammatory reaction (COX-2).

Prostaglandin PGE_2 is a strong pro-inflammatory mediator and also induces fever and pain. Compounds belonging to the classes usually denoted "NSAIDs" (Non-Steroidal Anti-Inflammatory Drugs) and "coxibs" (selective cyclooxygenase-2 inhibitors) act predominantly by inhibition of COX-1 and/or COX-2, thereby reducing the formation of the proinflammatory PGE_2. However, by inhibiting the cyclooxygenase(s) the production of all metabolites will be decreased. As some of these arachidonic acid metabolites have beneficial properties the inhibition of the cyclooxygenase(s) are causing, or are

suspected to cause, adverse biological effects. For example, the unselective inhibition of cyclooxygenase(s) by NSAIDs gives gastrointestinal (GI) side effects and affects platelet and renal function. The selective inhibition of COX-2 by the coxibs has reduced the frequency of GI side effects, but is instead believed to cause cardiovascular problems.

Thus, an agent that would selectively inhibit the transformation of PGH_2 to PGE_2 during inflammation is not expected to give rise to these unwanted side effects. The enzyme responsible for this transformation is the prostaglandin E_2 synthase (PGES). This enzyme exists in both a cytosolic and a membrane-associated form. Whereas the cytosolic enzyme is widely expressed and involved in formation of PGE_2 for various physiological effects, the membrane associated PGES is induced by proinflammatory cytokines and is responsible for the production of large amounts of PGE_2 during inflammation. This invention describes compounds that are selective inhibitors of the membrane-associated form of PGES, the mPGES.

mPGES belongs to the MAPEG (membrane-associated proteins in eicosanoid and glutathione metabolism) family, which has been defined according to enzymatic activities, sequence motifs and structural properties. Other members of the MAPEG family comprise the 5-lipoxygenase-activating protein(FLAP), leukotriene C_4 synthase, microsomal glutathione S-transferase 1 (MGST1), MGST2, and MGST3. Also these proteins are involved in the formation of arachidonic acid metabolites that may have profound biological activities.

Accordingly, blocking the effect of mPGES is equivalent to a pharmacological effect against inflammatory diseases and processes, and against diseases, disorders and conditions where pain or fever is present. Accordingly, selective mPGES inhibitors would be important for alleviating, preventing, inhibiting or treating a disease, disorder, or condition associated with inflammation, acute or chronic pain, or fever, such as: inflammatory bowel disease, irritable bowel syndrome, migraine, headache, low back pain, fibromyalgia, myofascial

disorders, viral infections (*e.g.* influenza, common cold, herpes zoster, and AIDS), bacterial infections, fungal infections, dysmenorrhea, burns, surgical or dental procedures, malignancies (*e.g.* breast cancer, colon cancer, and prostate cancer), atherosclerosis, gout, arthritis, osteoarthritis, juvenile arthritis, rheumatoid arthritis, rheumatic fever, ankylosing spondylitis, systemic lupus erythematosus, vasculitis, pancreatitis, nephritis, bursitis, conjunctivitis, iritis, scleritis, uveitis, wound healing, dermatitis, eczema, psoriasis, stroke, diabetes mellitus; neurodegenerative disorders such as Alzheimers disease and multiple sclerosis, autoimmune diseases, osteoporosis, asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, allergic disorders, and rhinitis.

In all of the above mentioned conditions, the mPGES inhibitors may be beneficial alone or in combination with other active drugs.

PRIOR ART

The present invention relates to indole-2-carboxylic acid, derivatives thereof, such as esters, amides, hydroxamic acids, or analogues thereof, such as 2-(hydroxymethyl)indoles, in which the indole skeleton is substituted in the 4, 5, 6, or 7-position with an aromatic group, and in which at the same time an aromatic residue is connected via a spacer to the indole nitrogen, and in which the indole skeleton is also substituted in the 3-position with an aromatic residue, or with an amide residue through its nitrogen atom.

WO 94/14434 from SmithKline Beecham claims certain indole-2-carboxylic acids as endothelin receptor antagonists and their use for treating hypertension, renal failure and cerebrovascular disease. Indoles which have an aromatic group in the indolic 3-position and at the same time an aromatic group in either the indolic 4-, 5-, 6-, or 7-position are covered by the general structure in the claims but are not examplified. It is unlikely that such compounds ever have been made and thus unknown if they are endothelin receptor antagonists.

WO 96/3377 from Sankyo claims certain indole-2-carboxylic acids as allosteric effectors at the muscarinic receptor. Altough indoles whith an aromatic group in the indolic 3-position which at the same time have an aromatic group in either the indolic 4-, 5-, 6-, or 7-position are claimed, the claims demands the absolute presence of a carboxyl group, a thiocarboxy group, a sulfonamide, a tetrazole or any of their protected analogues, etc, in the 4-, 5-, 6-, or 7-position that is not substituted by an aromatic group.

WO 99/43673 from Genetics Institute contains four independent very broad compound claims covering various indoles and indolines as phospholipase A_2 inhibitors and their use in inflammation *etc*. The extremely broad definitions in the claimes include some aspects claimed in the present application. However, there is neither one single compound with an aromatic group or an amide in the indolic 3-position included in the examples, nor is any route for their synthesis

described. It is unlikely that such compounds ever have been made and thus unknown if they are phospholipase A_2 inhibitors.

AstraZeneca has a number of patents and patent applications covering indole-2-carboxylic acids and their use in the treatment of disease mediated by monocyte chemoattractant protein-1 (MCP-1) or RANTES (Regulated upon Activation, Normal T-Cell Expressed and Secreted), such as inflammatory disease. The compound claims are very broad. For example, some applications claim "hydrocarbyl"-substituents in the benzenoid part of the molecules, where hydrocarbyl "refers to any structure comprising carbon and hydrogen atoms". Some of the patents or applications claim compounds with specific substituent in the 4-position *i.e.* amides or sulfonamides connected *via* their nitrogens or carbonates connected *via* an oxygen (WO 00/46195, EP 1159269), ethers, sulfones or sulfoxides (US 6569888, WO 00/46198), substituted alkyl or amides connected *via* the carbonyl-carbon (WO 00/46197), but compounds which have aromatic residues in the 5-, 6-, or the 7-position are not examplified. The claims in WO 00/46199 include a "hydrocarbyl" or a heteroaryl group in the 4-position, as well as in the 5-, 6-, or 7-positions. As before, compounds with aromatic residues in either the 4-, 5-, 6-, or 7-position are not examplified. The claims in all the patents and patent applications from this class, only covers compounds in which the 1-substituents is an aromatic moiety connected to the indole nitrogen through a CH_2 or a SO_2 linker. It is unlikely that compounds like the ones refered to in the present invention, *i.e.* compounds where there is an aromatic group in the indolic 4-, 5-, 6-, or 7-position, ever have been made, and it is thus unknown if they are active at MCP-1 or RANTES.

A related patent from Zeneca (US 6441004) claim compounds with aromatic residues in the benzenoid part of the indole skeleton, and such compounds are also examplified. However, the claims do not include aromatic or amide substituents in the indolic 3-position, and the examples only include 3-unsubstituted or 3-bromo-substituted compounds. Again, it is unlikely that

compounds as those described in the present application have been synthesized and tested.

There are a number of patents and patent applications that claim compounds that show some resemblance to the ones claimed in the present invention.

NMDA receptor antagonists which are indole-2-carboxylic acids with an amide functionality has been claimed by Merrel Dow for the use of various conditions and diseases (*e. g.* US 5189054). No compounds with an aromatic moiety directly connected to either the 4-, 5-, 6-, or the 7-position of the indole ring are claimed.

Compounds as PPAR-γ agonists for use in the treatment of obesity, diabetes, inflammation, *etc*, have been claimed by Merck in WO 01/30343. The claims covers indole-2-alkanoic acids, including indole-2-carboxylic acids, with aryl groups in the indole 3-position. No compounds with an aromatic moiety directly connected to either the 4-, 5-, 6-, or the 7-position of the indole ring are however claimed. A related patent (US 6525083) does not claim a carboxylic residue in the 2-position of the indole.

Merck Frosst claims indole-2-alkanoic acids as prostaglandin antagonists (EP 166591). Compounds with phenyl groups in the 3- and in the 4-, 5-, 6-, or the 7-position of the indole ring are included in the claims, but indole-2-carboxylic acids are not.

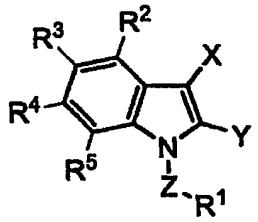
Merck Frosst also has a large number of patents and patent applications (*e.g.* US 5081138, EP 535924) that claims indole-2-alkanoic acids as inhibitors of FLAP (5-lipoxygenase-activating protein) as anti-asthmatic, anti-allergic, anti-inflammatory agents, *etc*. However, the claims do not cover the compounds described in the present application.

Pfizer has claimed indole compounds as COX-2 inhibitors (*e.g.* EP 985666, WO 99/05104). The claims covers indole-2-carboxylic acids with an amide connected *via* its nitrogen to the indolic 3-position. However, the compounds all lack a substituent in the indolic 1-position, and aromatic substituents in the 4-, 5-, 6-, or the 7-position of the indole ring are not claimed.

SUMMARY OF THE INVENTION

One object of the present invention is an indole-2-carboxylic acid, a derivative thereof, such as an ester, amide, hydroxamic acid, or an analogue thereof, such as a 2-(hydroxymethyl)indole, in which the indole skeleton is substituted in the 4, 5, 6, or 7-position with aryl or heteroaryl, and in which an aryl or a heteroaryl residue is connected via a spacer to the indole nitrogen, and in which the indole skeleton is substituted in the 3-position with an aryl or a heteroaryl residue, or with an amide residue through its nitrogen atom.

Another object of the present invention is a compound of formula (I):



(I)

wherein:

X is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) $R^6C(O)N(R^7)$–;

Y is selected from $HOCH_2$–, $(R^8)NHC(O)$–, $R^8ONHC(O)$–, and $R^8OC(O)$–;

Z is a C_{1-8}-alkylene chain or a heteroalkylene chain having 2 to 8 chain atoms, which optionally contains one or more unsaturations, wherein the C_{1-8}-alkylene chain and the heteroalkylene chain may be optionally substituted in one or more

positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, and O=; and wherein one or more atoms of the C_{1-8}-alkylene chain or the heteroalkylene chain are optionally part of an additional C_{3-8}-cycloalkyl-, or C_{3-8}-heterocycloalkyl-ring, where the said ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and optionally is substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, and O=;

R^1 is selected from aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

R^2, R^3, R^4, and R^5 are each independently selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

(iii) hydrogen, halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

or any adjacent pair of R^2, R^3, R^4, or R^5 may be part of an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

provided that at least one of R^2, R^3, R^4, or R^5 is aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

A is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

(iii) halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

B is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, and by an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

(iii) halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

R^6 and R^7 are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–,

O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

or where R^6 and R^7 are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

R^8, R^9, R^{10}, R^{11}, and R^{12} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(W)$–, $(R^{14})(R^{15})NC(W)$–, $R^{13}OC(W)$–, $R^{13}SC(W)$–, $(R^{14})(R^{15})N$–, $R^{13}C(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})C(W')N(R^{17})$–,

$R^{13}OC(W)N(R^{16})C(W')N(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})$–, $R^{13}SC(W)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})S(O)_qN(R^{17})$–, $R^{13}OC(W)N(R^{16})S(O)_qN(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})S(O)_qN(R^{17})$–, $R^{13}OS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(W)O$–, $(R^{14})(R^{15})NC(W)O$–, $R^{13}OC(W)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, and by an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^{13}–, $R^{13}O$–, and O=;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(W)$–, $(R^{14})(R^{15})NC(W)$–, $R^{13}OC(W)$–, $R^{13}SC(W)$–, $(R^{14})(R^{15})N$–, $R^{13}C(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})C(W')N(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})$–, $R^{13}SC(W)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})S(O)_qN(R^{17})$–, $R^{13}OC(W)N(R^{16})S(O)_qN(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})S(O)_qN(R^{17})$–, $R^{13}OS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(W)O$–, $(R^{14})(R^{15})NC(W)O$–, $R^{13}OC(W)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, S=, $R^{13}N$=, $(R^{14})(R^{15})NN$=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^{14})(R^{15})C$=;

or where any pair of R^8, R^9, R^{10}, R^{11}, and R^{12} are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–,

R^{13}–, $R^{13}C(W)$–, $(R^{14})(R^{15})NC(W)$–, $R^{13}OC(W)$–, $R^{13}SC(W)$–, $(R^{14})(R^{15})N$–, $R^{13}C(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})C(W')N(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})$–, $R^{13}SC(W)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})S(O)_qN(R^{17})$–, $R^{13}OC(W)N(R^{16})S(O)_qN(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})S(O)_qN(R^{17})$–, $R^{13}OS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(W)O$–, $(R^{14})(R^{15})NC(W)O$–, $R^{13}OC(W)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, S=, $R^{13}N$=, $(R^{14})(R^{15})NN$=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^{14})(R^{15})C$=;

R^{13}, R^{14}, R^{15}, R^{16} and R^{17} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $R^{18}SC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})C(O)N(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})$–, $R^{18}SC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})S(O)_qN(R^{22})$–, $R^{18}OC(O)N(R^{21})S(O)_qN(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})S(O)_qN(R^{22})$–, $R^{18}OS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–, $R^{18}OS(O)_qO$–, $R^{18}S$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $R^{18}SC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})C(O)N(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})$–, $R^{18}SC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})S(O)_qN(R^{22})$–, $R^{18}OC(O)N(R^{21})S(O)_qN(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})S(O)_qN(R^{22})$–, $R^{18}OS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–, $R^{18}OS(O)_qO$–, $R^{18}S$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, O=, S=, $R^{18}N$=, $(R^{19})(R^{20})NN$=, $R^{18}ON$=, $(R^{19})(R^{20})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^{19})(R^{20})C$=;

or where any pair of R^{13}, R^{14}, R^{15}, R^{16} and R^{17} are optionally joined to form a 5-7 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $R^{18}SC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})C(O)N(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})$–, $R^{18}SC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})S(O)_qN(R^{22})$–, $R^{18}OC(O)N(R^{21})S(O)_qN(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})S(O)_qN(R^{22})$–, $R^{18}OS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–, $R^{18}OS(O)_qO$–, $R^{18}S$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, O=, S=, $R^{18}N$=, $(R^{19})(R^{20})NN$=, $R^{18}ON$=, $(R^{19})(R^{20})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^{19})(R^{20})C$=;

R^{18}, R^{19}, R^{20}, R^{21} and R^{22} are each independently selected from:

(i) hydrogen;

(ii) C_{1-6}-alkyl, optionally substituted in one or more positions by one or more halogens, H_2N–, MeHN–, EtHN–, *i*-PrHN–, Me_2N–, Et(Me)N–, *i*-Pr(Me)N–, Et_2N–, HO–, MeO–, EtO–, *i*-PrO– or =O;

Q and Q' are substituents connected by a double bond, and are each independently selected from:

O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

W and W' are substituents connected by a double bond, and are each independently selected from:

O=, S=, $R^{13}N$=, $(R^{14})(R^{15})NN$=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^{14})(R^{15})C$=;

q is 1 or 2;

as well as pharmaceutically acceptable salts, stereoisomers or prodrugs thereof.

A preferred embodiment of the present invention relates to compounds according to the general formula (I), wherein ;

X is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) $R^6C(O)N(R^7)$–;

Y is selected from $(R^8)NHC(O)–$, $R^8ONHC(O)–$, and $R^8OC(O)–$;

Z is a C_{1-8}-alkylene chain or a heteroalkylene chain having 2 to 8 chain atoms, which optionally contains one or more unsaturations, wherein the C_{1-8}-alkylene chain and the heteroalkylene chain may be optionally substituted in one or more positions by one or more groups independently selected from halogen, $R^8–$, $(R^9)(R^{10})N–$, $R^8O–$, and O=; and wherein one or more atoms of the C_{1-8}-alkylene chain or the heteroalkylene chain are optionally part of an additional C_{3-8}-cycloalkyl-, or C_{3-8}-heterocycloalkyl-ring, where the said ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and optionally is substituted in one or more positions by one or more groups independently selected from halogen, $R^8–$, $(R^9)(R^{10})N–$, $R^8O–$, and O=;

R^1 is selected from aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

R^2, R^3, R^4, and R^5 are each independently selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, $R^8–$, $R^8C(Q)–$, $(R^9)(R^{10})NC(Q)–$, $R^8OC(Q)–$, $R^8SC(Q)–$, $(R^9)(R^{10})N–$, $R^8C(Q)N(R^{11})–$, $(R^9)(R^{10})NC(Q)N(R^{11})–$, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})–$, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})–$, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})–$, $R^8OC(Q)N(R^{11})–$, $R^8SC(Q)N(R^{11})–$, $N_3–$, $O_2N–$, $R^8S(O)_qN(R^{11})–$, $(R^9)(R^{10})NS(O)_qN(R^{11})–$,

$(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

(iii) hydrogen, halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

or any adjacent pair of R^2, R^3, R^4, or R^5 may be part of an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

provided that at least one of R^2, R^3, R^4, or R^5 is aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

A is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

(iii) halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

B is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, and by an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, or O=;

R^6 and R^7 are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B,

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

or where R^6 and R^7 are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–,

R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

R^8, R^9, R^{10}, R^{11}, and R^{12} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–,$(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, and by an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^{13}–, $R^{13}O$–, and O=;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-hetero-cycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, $(R^{14})(R^{15})NN$=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

or where any pair of R^8, R^9, R^{10}, R^{11}, and R^{12} are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, $(R^{14})(R^{15})NN$=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

R^{13}, R^{14}, R^{15}, and R^{16} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $R^{18}OC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–, $R^{18}OS(O)_qO$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $R^{18}OC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–,

$R^{18}OS(O)_qO$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, O=, $(R^{19})(R^{20})NN$=, $R^{18}ON$=, $(R^{19})(R^{20})NS(O)_2N$=, NCN=, and O_2NCH=;

or where any pair of R^{13}, R^{14}, R^{15} and R^{16} are optionally joined to form a 5-7 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1 unsaturation, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $R^{18}OC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–, $R^{18}OS(O)_qO$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, O=, $(R^{19})(R^{20})NN$=, $R^{18}ON$=, $(R^{19})(R^{20})NS(O)_2N$=, NCN=, and O_2NCH=;

R^{18}, R^{19}, R^{20}, and R^{21} are each independently selected from:

(i) hydrogen;

(ii) C_{1-6}-alkyl, optionally substituted in one or more positions by one or more halogens, H_2N–, MeHN–, EtHN–, *i*-PrHN–, Me_2N–, Et(Me)N–, *i*-Pr(Me)N–, Et_2N–, HO–, MeO–, EtO–, *i*-PrO– or =O;

Q and Q' are substituents connected by a double bond, and are each independently selected from:

O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

q is 1 or 2;

as well as pharmaceutically acceptable salts, stereoisomers or prodrugs thereof.

A more preferred embodiment is ;

X is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) $R^6C(O)N(R^7)$–;

Y is selected from $(R^8)NHC(O)$–, and $R^8OC(O)$–;

Z is a C_{1-8}-alkylene chain or a heteroalkylene chain having 2 to 8 chain atoms, which optionally contains one or more unsaturations, wherein the C_{1-8}-alkylene chain and the heteroalkylene chain may be optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, or O=; and wherein one or more atoms of the C_{1-8}-alkylene chain or the heteroalkylene chain are optionally part of an additional C_{3-8}-cycloalkyl-, or C_{3-8}-heterocycloalkyl-ring, where the said ring optionally contains 1-2 heteroatoms and optionally 1 unsaturation, and optionally is substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, and O=;

R^1 is selected from aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

R^2, R^3, R^4, and R^5 are each independently selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) hydrogen, halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

or any adjacent pair of R^2, R^3, R^4, or R^5 may be part of an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

provided that at least one of R^2, R^3, R^4, or R^5 is aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

A is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

B is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–,

R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

R^6 and R^7 are each independently selected from:

(i) hydrogen,

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

or where R^6 and R^7 are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1 unsaturation, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

R^8, R^9, R^{10}, and R^{11} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–,

$R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

or where any pair of R^8, R^9, R^{10}, and R^{11} are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

R^{13}, R^{14}, R^{15}, and R^{16} are each independently selected from:

(i) hydrogen;

(ii) C_{1-6}-alkyl, optionally substituted in one or more positions by one or more halogens, H_2N–, MeHN–, EtHN–, *i*-PrHN–, Me_2N–, Et(Me)N–, *i*-Pr(Me)N–, Et_2N–, HO–, MeO–, EtO–, *i*-PrO– or =O;

q is 1 or 2;

as well as pharmaceutically acceptable salts, stereoisomers or prodrugs thereof.

A particularly preferred embodiment of the present invention relates to compounds according to the general formula (I), wherein ;

X is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) $R^6C(O)N(R^7)$–;

Y is $R^8OC(O)$–;

Z is a C_{1-8}-alkylene chain or a heteroalkylene chain having 2 to 8 chain atoms, which optionally contains one or more unsaturations, wherein the C_{1-8}-alkylene chain and the heteroalkylene chain may be optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, or O=; and wherein one or two carbon atoms of the C_{1-8}-alkylene chain or the heteroalkylene chain may be common to an additional cyclopropyl ring;

R^1 is selected from aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

R^2, R^3, R^4, and R^5 are each independently selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) hydrogen, halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, and $R^8OS(O)_2$–;

or any adjacent pair of R^2, R^3, R^4, or R^5 may be part of a methylenedioxy, difluoromethylenedioxy, or dimethylmethylenedioxy residue;

provided that at least one of R^2, R^3, R^4, or R^5 is aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

A is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

B is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

R^6 and R^7 are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–,

R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

or where R^6 and R^7 are optionally joined to form a 5-6 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1 unsaturation, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

R^8, R^9, R^{10}, and R^{11} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_2N(R^{16})$–, $(R^{14})(R^{15})NS(O)_2N(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_2O$–, $(R^{14})(R^{15})NS(O)_2O$–, $R^{13}OS(O)_2O$–, $R^{13}S(O)_2$–, $(R^{14})(R^{15})NS(O)_2$–, $R^{13}OS(O)_2$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–,

$R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_2N(R^{16})$–, $(R^{14})(R^{15})NS(O)_2N(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_2O$–, $(R^{14})(R^{15})NS(O)_2O$–, $R^{13}OS(O)_2O$–, $R^{13}S(O)_2$–, $(R^{14})(R^{15})NS(O)_2$–, $R^{13}OS(O)_2$–, O=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

or where any pair of R^8, R^9, R^{10}, and R^{11} are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1 unsaturation, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_2N(R^{16})$–, $(R^{14})(R^{15})NS(O)_2N(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_2O$–, $(R^{14})(R^{15})NS(O)_2O$–, $R^{13}OS(O)_2O$–, $R^{13}S(O)_2$–, $(R^{14})(R^{15})NS(O)_2$–, $R^{13}OS(O)_2$–, O=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

R^{13}, R^{14}, R^{15}, and R^{16} are each independently selected from:

(i) hydrogen;

(ii) C_{1-6}-alkyl, optionally substituted in one or more positions by one or more halogens, H_2N–, MeHN–, EtHN–, *i*-PrHN–, Me_2N–, Et(Me)N–, *i*-Pr(Me)N–, Et_2N–, HO–, MeO–, EtO–, *i*-PrO– or =O;

as well as pharmaceutically acceptable salts, stereoisomers or prodrugs thereof.

Especially preferred are the following compounds:

(E1): 6-(4-*tert*-Butylphenyl)-1-(3-phenoxybenzyl)-3-phenylindole-2-carboxylic acid;

(E2): 6-(4-*tert*-Butylphenyl)-1-(3-phenoxybenzyl)-3-(2-thienyl)indole-2-carboxylic acid;

(E3): 5-(3,4-methylenedioxyphenyl)-3-phenyl-1-(3-phenylpropyl)indole-2-carboxylic acid;

(E4): 3-Phenyl-1-(3-phenylpropyl)-5-(3-pyridinyl)indole-2-carboxylic acid;

(E5): 6-(4-Benzyloxyphenyl)-3-(3-carboxyphenyl)-1-(3-nitrobenzyl)indole-2-carboxylic acid;

(E6): 3-(3-Carboxyphenyl)-4-phenyl-1-(3-trifluoromethylbenzyl)indole-2-carboxylic acid;

(E7): 6-(4-Benzyloxyphenyl)-1-(3-nitrobenzyl)-3-(2-oxopyrrolidin-1-yl)indole-2-carboxylic acid;

(E8): 3-(2-Oxopyrrolidin-1-yl)-1-(3-phenoxybenzyl)-5-phenylindole-2-carboxylic acid;

(E9): 1-(3,5-Difluorobenzyl)-4-methoxy-3-(2-oxopyrrolidin-1-yl)-7-phenylindole-2-carboxylic acid;

(E10): 6-(3,4-Methylenedioxyphenyl)-1-(3,5-bis-trifluoromethylbenzyl)-3-(4-chlorobenzoylamino)indole-2-carboxylic acid;

(E11): 3-(3,5-Dimethoxybenzoylamino)-5-(4-nitrophenyl)-1-(3-phenoxybenzyl)-indole-2-carboxylic acid;

(E12): 3-(3-Amino-4-methylbenzoylamino)-5-(4-*tert*-butylphenyl)-1-(3-chloro-benzyl)indole-2-carboxylic acid;

(E13): 5-(4-*tert*-Butylphenyl)-1-(3-chlorobenzyl)-3-[(pyridine-3-carbonyl)-amino]indole-2-carboxylic acid;

(E14): 3-(4-dimethylaminobutyrylamino)-6-(3,4-methylenedioxyphenyl)-1-(3-phenoxybenzyl)indole-2-carboxylic acid;

(E15): 1-(3-Cyanobenzyl)-6-(3,4-methylenedioxyphenyl)-3-(3-phenylacryloyl-amino)indole-2-carboxylic acid;

(E16): 1-(3-Carbamoylbenzyl)-6-(3,4-methylenedioxyphenyl)-3-(3-phenyl-acryloylamino)indole-2-carboxylic acid;

(E17): 3-Acetylamino-5-(3,4-methylenedioxyphenyl)-1-(5-phenoxy-pentyl)indole-2-carboxylic acid;

(E18): 5-(3,4-Methylenedioxyphenyl)-3-(2-oxopiperidin-1-yl)-1-(5-phenoxy-pentyl)indole-2-carboxylic acid;

as well as pharmaceutically acceptable salts, stereoisomers or prodrugs thereof.

Another object of the present invention is a compound as defined above for medical use.

Another object of the present invention is a pharmaceutical composition comprising a compound as defined above together with a pharmaceutical diluent or carrier.

Another object of the present invention is a process for preparation of the pharmaceutical composition as defined above by combining a compound as defined above together with a pharmaceutical diluent or carrier.

Another object of the present invention is a method for alleviating, preventing, inhibiting, or treating a disease associated with inflammation, pain, or fever by administering to a subject in need of treatment thereof, a therapeutically effective amount of a compound of formula (I).

Another object of the present invention is a method for alleviating, preventing, inhibiting, or treating a disease, disorders, or condition, which can be modulated by inhibition of mPGES, by administering to a subject in need of treatment thereof, a therapeutically effective amount of a compound of formula (I).

The diseases, disorders, or conditions referred to comprise inflammatory bowel disease, inflammatory pain, pain, migraine, headache, viral infections (e.g. influenza, common cold, and AIDS), bacterial infections, dysmenorrhea, burns, surgical or dental procedures, atherosclerosis, gout, arthritis, osteoarthritis, juvenile arthritis, rheumatoid arthritis, rheumatic fever, ankylosing spondylitis, systemic lupus erythematosus, vasculitis, pancreatitis, nephritis, bursitis,

conjunctivitis, iritis, scleritis, uveitis, wound healing, dermatitis, eczema, psoriasis, stroke, diabetes, autoimmune diseases, Alzheimers disease, multiple sclerosis, malignancies, asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, allergic disorders, and rhinitis.

Another embodiment of the invention is a method for inhibiting mPGES in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of any of the compounds or any of the pharmaceutical compositions described herein.

The compounds of the invention are mPGES inhibitors and as such may be useful in the treatment of inflammatory bowel disease, irritable bowel syndrome, migraine, headache, low back pain, fibromyalgia, myofascial disorders, viral infections (*e.g.* influenza, common cold, herpes zoster, and AIDS), bacterial infections, fungal infections, dysmenorrhea, burns, surgical or dental procedures, malignancies (*e.g.* breast cancer, colon cancer, and prostate cancer), atherosclerosis, gout, arthritis, osteoarthritis, juvenile arthritis, rheumatoid arthritis, rheumatic fever, ankylosing spondylitis, systemic lupus erythematosus, vasculitis, pancreatitis, nephritis, bursitis, conjunctivitis, iritis, scleritis, uveitis, wound healing, dermatitis, eczema, psoriasis, stroke, diabetes mellitus; neurodegenerative disorders such as Alzheimers disease and multiple sclerosis, autoimmune diseases, osteoporosis, asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, allergic disorders, and rhinitis (alone or in combination with analgesics, anti-inflammatory compounds, antipyretics, antimigrainics, antirheumatics, antitussives, antihyperlipoproteinemics, antiparkinsonians, nootropics, antibacterials, antivirals, antimycotica, antiallergics, nitric oxide releasing drugs, immunomodulators, immunosuppresants, cytostatica, chemotherapy, and hormone therapy).

Another object of the present invention is a method for eliciting a mPGES modulating effect in a subject in need of treatment, which comprises

administering to the subject of a therapeutically effective amount of a compound of formula (I).

The compounds of the present invention in labelled form, *e. g.* isotopically labelled, may be used as diagnostic agents.

Another object of the present invention is the use of a compound of formula (I) in the manufacture of a medicament for the therapeutic alleviation, treatment or prevention of a disease, disorder, or condition, which is associated with mPGES in a subject in need thereof.

Examples of such diseases and disorders are inflammatory bowel disease, irritable bowel syndrome, migraine, headache, low back pain, fibromyalgia, myofascial disorders, viral infections (*e.g.* influenza, common cold, herpes zoster, and AIDS), bacterial infections, fungal infections, dysmenorrhea, burns, surgical or dental procedures, malignancies (*e.g.* breast cancer, colon cancer, and prostate cancer), atherosclerosis, gout, arthritis, osteoarthritis, juvenile arthritis, rheumatoid arthritis, rheumatic fever, ankylosing spondylitis, systemic lupus erythematosus, vasculitis, pancreatitis, nephritis, bursitis, conjunctivitis, iritis, scleritis, uveitis, wound healing, dermatitis, eczema, psoriasis, stroke, diabetes mellitus; neurodegenerative disorders such as Alzheimers disease and multiple sclerosis, autoimmune diseases, osteoporosis, asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, allergic disorders, and rhinitis.

DETAILED DESCRIPTION OF THE INVENTION

The following definitions apply to the terms as used throughout this specification, unless otherwise limited in specific instances. All publications mentioned herein are hereby incorporated by reference.

The expressions "comprise" and "comprising" mean "including but not limited to".

The term "mPGES inhibitor" as used herein is intended to cover any moiety that prevents the action of the mPGES enzyme, or a complex of which the mPGES enzyme forms a part.

The term "subject" as used herein refers to a patient, which may *e.g.* be a mammal including human beings.

The term "effective amount" refers to an amount of a compound, which confers a therapeutic effect on the treated subject. The therapeutic effect may be objective (*i.e.* measurable by some test or marker) or subjective (*i.e.* the subject gives an indication of or feels an effect).

The term "spacer", as used herein alone or as part of another group, refers to a group that connects one residue to another. Exemplary spacers include, but are not restricted to, optionally substituted alkylene or heteroalkylene chains.

The term "halogen", as used herein alone or as part of another group, refers to chlorine, bromine, fluorine, and iodine.

The term "heteroatom" as used herein, refers to nitrogen, oxygen, sulphur, and in heterocyclic rings, also selenium.

The term "C_{1-6}-alkyl", as used herein alone or as part of another group, refers to an alkyl group which may be straight or branched. Exemplary C_{1-6}-alkyl groups include, but are not restricted to, methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *sec*-butyl, isobutyl, *tert*-butyl, *n*-pentyl, isopentyl, *n*-hexyl, and isohexyl.

The term "C_{3-8}-cycloalkyl", as used herein alone or as part of another group, refers to a mono-, or bicyclic alkyl group, which may contain one or more

unsaturations (double, and/or triple bonds). Exemplary C_{3-8}-cycloalkyl groups include, but are not restricted to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclopentenyl, cyclohexenyl, cycloheptenyl, cyclooctenyl, cyclooctynyl, bicycloheptyl, bicyclooctyl, and bicyclooctenyl. It is understood that a single carbon of the C_{3-8}-cycloalkyl may be common to another C_{3-8}-cycloalkyl or C_{3-8}-heterocycloalkyl, forming a so called spiro-compound. It is also understood that a single carbon of the C_{3-8}-cycloalkyl may be common to a carbon in *e.g.* an alkylgroup.

The term "C_{2-6}-alkenyl", as used herein alone or as part of another group, refers to an alkenyl group which may be straight or branched. Exemplary C_{2-6}-alkenyl groups include, but are not restricted to, vinyl, 1-propenyl, 2-propenyl, propadienyl, 1-butenyl, 2-butenyl, 3-butenyl, 1,3-butadienyl, 1-pentenyl, 2-pentenyl, 4-pentenyl, and 5-hexenyl.

The term "C_{2-6}-alkynyl", as used herein alone or as part of another group, refers to an alkynyl group which may be straight or branched. Exemplary C_{2-6}-alkynyl groups include, but are not restricted to, ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 2-butynyl, 3-butynyl, 1-pentynyl, 2-butynyl, 4-pentynyl, 1-hexynyl, 3-hexynyl, and 5-hexynyl.

The term "C_{3-8}-heterocycloalkyl", as used herein alone or as part of another group, refers to a mono-, or bicyclic alkyl group which may contain one or more heteroatoms, and which may contain one or more unsaturations (double, and/or triple bonds). Exemplary C_{3-8}-heterocycloalkyl groups include, but are not restricted to, aziridine, azetidine, pyrrolidine, pyrroline, piperidine, tetrahydropyridine, dihydropyridine, pyrazolidine, imidazolidine, imidazoline, piperazine, morpholine, thiomorpholine, oxirane, oxetane, tetrahydrofuran, pyran, dihydropyran, tetrahydropyran, 1,3-dioxolane, 1,3-dioxane, 1,4-dioxane, thiirane, thietane, thiolane, 1,3-dithiolane, 1,4-dithiane, 1,3,5-trithiane, quinuclidine, and tropane. It is understood that a single carbon or nitrogen of the C_{3-8}-heterocycloalkyl may be common to another C_{3-8}-cycloalkyl-, or C_{3-8}-

heterocycloalkyl-group, forming a so called spiro-compound. It is also understood that a single carbon or nitrogen of the C_{3-8}-heterocycloalkyl may be common to a carbon or nitrogen in *e.g.* an alkylgroup.

The term "aryl" is intended to include monocyclic or bicyclic ring systems having from 6 to 10 ring carbon atoms, in which at least one ring is aromatic. Examples of such ring systems are benzene, naphtalene, 1,2,3,4-tetrahydro-naphtalene, indan, and indene.

The term "heteroaryl" refers to a mono-, bi- or tricyclic ring system having from 5 to 10 ring atoms, in which at least one ring is aromatic, and in which one or more of the ring atoms are other than carbon, such as nitrogen, sulphur, oxygen and selenium. Examples of such heteroaryl rings include, but are not restricted to, pyrrole, furan, thiophene, pyrazole, imidazole, oxazole, isoxazole, thiazole, isothiazole, 1,2,3-triazole, 1,2,4-triazole, 1,3,4-triazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,3,4-thiadiazole, tetrazole, pyridine, indole, isoindole, indoline, isoindoline, quinoline, 1,2,3,4-tetrahydroquinoline, isoquinoline, 1,2,3,4-tetrahydroisoquinoline, quinolizine, carbazole, acridine, benzofuran, isobenzofuran, chroman, isochroman, benzothiophene, pyridazine, pyrimidine, pyrazine, indazole, benzimidazole, cinnoline, quinazoline, quinoxaline, phthalazine, 1,5-naphthyridine, 1,8-naphthyridine, phenazine, benzoxazole, 3,4-dihydro-2*H*-1,4-benzoxazine, benzothiazole, phenothiazine, 1,3-benzodioxole, benzodioxane, 2,1,3-benzoxadiazole, 2,1,3-benzothiazole, 2,1,3-benzoselena-diazole, purine, and pteridine. The ring system may be linked to the rest of the molecule via a carbon or nitrogen atom thereof.

The term "C_{1-8}-alkylene chain", as used herein alone or as part of another group, refers to an alkyl chain of 1 to 8 carbon atoms which is substituted at each end and includes methylene ($-CH_2-$), ethylene ($-CH_2CH_2-$), $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2CH_2CH_2CH_2-$, and

$-CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2-$.

The term "heteroalkylene chain", as used herein alone or as part of another group, refers to a C_{1-8}-alkylene chain, as defined above, where one or more carbons are substituted by heteroatoms. Exemplary heteroalkylene chains include, but are not restricted to: $-CH_2O-$, $-OCH_2-$, $-CH_2CH_2O-$, $-CH_2OCH_2-$, $-OCH_2CH_2-$, $-CH_2CH_2CH_2O-$, $-CH_2CH_2OCH_2-$, $-CH_2OCH_2CH_2-$, $-OCH_2CH_2CH_2-$, $-OCH_2CH_2O-$, $-CH_2CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2OCH_2-$, $-CH_2CH_2OCH_2CH_2-$, $-OCH_2CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2CH_2OCH_2-$, $-CH_2CH_2CH_2OCH_2CH_2-$, $-CH_2CH_2OCH_2CH_2CH_2-$, $-OCH_2CH_2CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2CH_2CH_2OCH_2-$, $-CH_2CH_2CH_2CH_2OCH_2CH_2-$, $-CH_2CH_2CH_2OCH_2CH_2CH_2-$, $-CH_2CH_2OCH_2CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2CH_2CH_2OCH_2CH_2-$, $-CH_2CH_2CH_2CH_2OCH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2OCH_2CH_2O-$, $-CH_2CH_2OCH_2CH_2OCH_2CH_2-$, $-CH_2NH-$, $-NHCH_2-$, $-CH_2CH_2NH-$, $-NHCH_2CH_2-$, $-CH_2CH_2CH_2NH-$, $-CH_2CH_2CH_2CH_2NH-$, $-CH_2CH_2CH_2CH_2CH_2CH_2NH-$, $-CH_2CH_2OCH_2CH_2NH-$, $-CH_2CH_2NHCH_2CH_2O-$, $-CH_2CH_2NHCH_2CH_2NH-$, $-CH_2S-$, $-CH_2CH_2S-$, $-CH_2CH_2OCH_2CH_2S-$, $-CH_2CH_2SCH_2CH_2O-$, $-CH_2CH_2NHCH_2CH_2S-$, and $-CH_2CH_2SCH_2CH_2NH-$.

The compounds of formula (I) in the invention may contain at least one chiral center and may therefore exist as optical isomers. The invention therefore comprises optically inactive racemic (*rac*) mixtures (a one to one mixture of enantiomers), optically enriched (scalemic) mixtures as well as optically pure individual enantiomers. The compounds in the invention also may contain more than one chiral center and therefore may exist as diastereomers. The invention therefore comprises individual diastereomers as well as any mixture of diastereomers.

The compound of formula (I) in the invention may contain geometrical isomers and may therefore exist as either the *E* (entgegen) or *Z* (zusammen) isomers. The invention therefore comprises individual E or Z isomers as well as any mixture of E and Z isomers.

The compound of formula (I) in the invention may exist in tautomeric forms; the invention therefore comprises the individual tautomeric forms as well as any mixture thereof.

Also included within the scope of the invention are polymorphs, hydrates, and solvates of the compounds of the instant invention.

The compounds of formula (I) can be present as salts, in particular pharmaceutically acceptable salts. The term "Pharmaceutically Acceptable Salts" refers to salts prepared from pharmaceutically acceptable non-toxic bases or acids including inorganic or organic bases and inorganic or organic acids. Salts derived from inorganic bases include aluminium, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganic salts, manganous, potassium, sodium, zinc salts, and the like. Particularly preferred are the ammonium, calcium, magnesium, potassium, and sodium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, and basic ion exchange resins, such as arginine, betaine, caffeine, choline, *N,N'*-dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, *N*-ethylmorpholine, *N*-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine, and the like. When the compound of this invention is basic, salts may be prepared from pharmaceutically acceptable non-toxic acids, including inorganic and organic acids. Such acids include, but are not restricted to, acetic,

benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, malonic, mandelic, methanesulfonic, mucic, nitric, pamoic, panthothenic, phosphoric, succinic, sulfuric, tartaric, and p-toluenesulfonic acid. Particularly preferred are citric, hydrobromic, hydrochloric, maleic, nitric, phosphoric, sulfuric, and tartaric acids. Salts in the solid form may exist in more than one crystal structure, and may also be in the form of solvates such as hydrates.

The present invention includes within its scope prodrugs of the compounds of this invention. In general, such prodrugs will be functional derivatives of the compounds of this invention which are readily convertible *in vivo* into the required compound. Thus, in the methods of treatment of the present invention, the term "administering" shall encompass the treatment of the various conditions described with the compound specifically disclosed or with a compound which may not be specifically disclosed, but which converts to the specified compound *in vivo* after administration to the patient. Conventional procedures for the selection and preparation of suitable prodrug derivatives are described, for example in "Design of Prodrugs" ed. H. Bundgaard, Elsevier, 1985, which is incorporated by reference herein in its entirety.

The present invention includes within its scope metabolites of compounds of formula (I). Metabolites of the compounds include active species produced upon introduction of compounds of this invention into the biological milieu.

The present invention includes within its scope compounds of formula (I) in an isotopically labeled form.

The compounds of the present invention can be administered in such oral dosage forms as tablets, capsules (each of which includes sustained release or timed release formulations), pills, powder, granules, elixirs, tinctures, suspensions, syrups and emulsions. Likewise, they may also be administered in intravenous (bolus or infusion), intraperitoneal, topical (*e.g.* ocular eyedrop),

subcutaneous, intramuscular, intraspinal, epidural, intranasal, buccal, or transdermal form, all using forms well known to those of ordinary skill in the pharmaceutical arts.

The dosage regimen utilizing the compounds of the present invention is selected in accordance with a variety of factors including type, species, age, weight, sex, and medical condition of the patient; the severity of the condition to be treated; the route of administration; the renal and hepatic function of the patient; and the particular compound or salt thereof employed. An ordinarily skilled physician, veterinarian or clinician can readily determine and prescribe the effective amount of the drug required to prevent, counter or arrest the progress of the condition.

Oral dosages of the present invention, when used for the indicated effects, will range between about 0.01 mg per kg of body weight per day (mg/kg/day) to about 100 mg/kg/day, preferably 0.01 mg per kg of body weight per day (mg/kg/day) to 10 mg/kg/day, and most preferably 0.1 to 5.0 mg/kg/day. For oral administration, the compositions are preferably provided in the form of tablets containing 0.01, 0.05, 0.1, 0.5, 1.0, 2.5, 5.0, 10.0, 15.0, 25.0, 50.0, 100, or 500 milligrams of the active ingredient for the symptomatic adjustment of the dosage to the patient to be treated. A medicament typically contains from about 0.01 mg to about 500 mg of the active ingredient, preferably from about 1 mg to about 100 mg of active ingredient. Intravenously, the most preferred doses will range from about 0.1 to about 10 mg/kg/minute during a constant rate infusion. Advantageously, compounds of the present invention may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three or four times daily. Furthermore, preferred compounds for the present invention can be administered in intranasal form *via* topical use of suitable intranasal vehicles, or *via* transdermal routes, using those forms of transdermal skin patches or iontophoretic devices well known to those of ordinary skill in the art. To be administered in the form of a

transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen.

In the methods of the present invention, the compounds herein described in detail can form the active ingredient, and are typically administered in admixture with suitable pharmaceutical diluents, exipients or carriers (collectively referred to herein as "carrier" materials) suitably selected with respect to the intended form of administration, that is, oral tablets, capsules, elixirs, syrups and the like, and consistent with conventional pharmaceutical practices.

For instance, for oral administration in the form of a tablet or capsule, the active drug component can be combined with an oral, non-toxic, pharmaceutically acceptable, inert carrier such as lactose, starch, sucrose, glucose, colloidal silicon dioxide, microcrystalline cellulose, methyl cellulose, sodium starch glycolate, magnesium stearate, calcium hydrogen phosphate, dicalcium phosphate, calcium sulfate, mannitol, sorbitol, and the like; for oral administration in liquid form, the oral drug components can be combined with any oral, non-toxic, pharmaceutically acceptable inert carrier such as ethanol, glycerol, water, and the like. Moreover, when desired or necessary, suitable binders, lubricants, disintegrating agents and coloring agents can also be incorporated into the mixture. Suitable binders include starch, gelatin, natural sugars such as glucose or beta-lactose, corn sweeteners, natural and synthetic gums such as acacia, tragacanth or sodium alginate, carboxymethylcellulose, polyethylene glycol, waxes, and the like. Lubricants used in these dosage forms include sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride, and the like. Disintegrators include without limitation starch, methylcellulose, agar, bentonite, xanthan gum, and the like.

The compounds of the present invention can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar

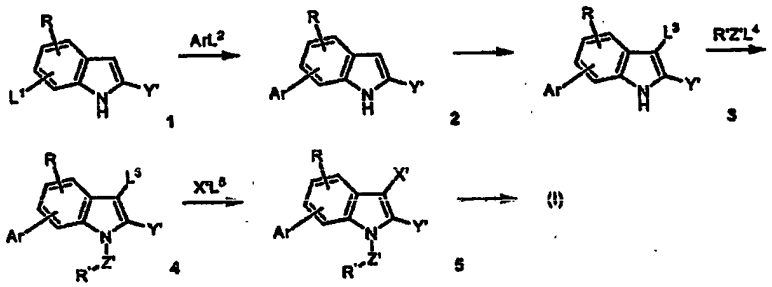
vesicles and multilamellar vesicles. Liposomes can be formed from *e. g.* phospholipids, cholesterol, stearylamine, or phosphatidylcholines.

The compounds of formula (I) may be prepared by the exemplary processes described in the following reaction schemes. Exemplary reagents and procedures for these reactions appear hereinafter and in the working Examples.

Scheme 1 describes a synthetic route that begins with a coupling reaction between an appropriately substituted indole **1**, and a reagent containing an aromatic residue Ar, giving the intermediate **2**. The leaving group L^1 on compound **1** is *e.g.* chloro, bromo, iodo, CF_3SO_2O–, $(HO)_2B$–, 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl, Bu_3Sn–, or a similar group known to those skilled in the art. The leaving group L^2 on ArL^2 is *e.g.* chloro, bromo, iodo, CF_3SO_2O–, $(HO)_2B$–, 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl, Bu_3Sn–, or a similar group known to those skilled in the art. It is understood that L^1 and L^2 are selected based on their mutual compatibility. The coupling reaction is preferably catalyzed by a mixture that may contain a metal, or a salt or complex thereof, such as CuI, Pd on carbon, $Pd(OAc)_2$, $Pd(Ph_3P)_2Cl_2$, $Pd(Ph_3P)_4$, or $NiCl_2$, a ligand such as *t*-Bu_3P, $(C_6H_{11})_3P$, Ph_3P, 1,2-bis(diphenylphosphino)-ethane, 2,2'-bis(di-*tert*-butylphosphino)-1,1'-biphenyl or 2,2'-bis(diphenylphosphino)-1,1'-binaphtyl, and a base such as, Na_2CO_3, K_3PO_4, Cs_2CO_3, or *t*-BuOK, or another mixture known to those skilled in the art. A leaving group L^3, such as bromo, iodo, or a similar group known to those skilled in the art, is introduced into **2** by a reagent, *e.g. N*-bromosuccinimide, iodine, or a mixture of NaI and *N*-chlorosuccinimide, affording the intermediate **3**. The substituent in the indolic 1-position is introduced into **3** using a reagent $R'Z'L^4$ which affords compound **4**. The leaving group L^4 is *e.g.* chloro, bromo, iodo, CF_3SO_2O–, TsO–, or a similar group known to those skilled in the art. The reaction is preferably performed in the presence of a base such as K_2CO_3, NaH, LDA, Et_3N, DMAP/pyridine, or a similar reagent known to those skilled in the art. Compound **5** is formed by introducing the substituent X' on **4**. If X' is an aromatic group, L^5 is $(HO)_2B$–, 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl,

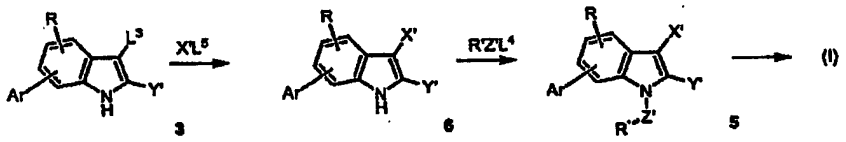
Bu_3Sn–, or a similar group known to those skilled in the art. It is understood that L^5 and X' are selected based on their mutual compatibility. The reaction is preferably catalyzed by a mixture that may contain a transition metal, or a salt or complex thereof, such as CuI, Pd on carbon, $Pd(OAc)_2$, $Pd(Ph_3P)_2Cl_2$, $Pd(Ph_3P)_4$, or $NiCl_2$, a ligand such as, *t*-Bu_3P, $(C_6H_{11})_3P$, Ph_3P, 1,2-bis(diphenylphosphino)ethane, 2,2'-bis(di-*tert*-butylphosphino)-1,1'-biphenyl or 2,2'-bis(diphenylphosphino)-1,1'-binaphtyl, and a base such as Na_2CO_3, K_3PO_4, Cs_2CO_3, or *t*-BuOK, or another mixture known to those skilled in the art. If X' is an amide group, L^5 is H, and the reaction is preferably performed in the presence of a system that may contain a metal, or a salt or complex thereof, such as Cu, $Cu(OAc)_2$, CuI, $Pd(OAc)_2$, or $NiCl_2$, an additive such as, Et_3N, pyridine, N,N'-dimethylethylenediamine, Ph_3P, or 2,2'-bis(diphenylphosphino)-1,1'-binaphtyl, and a base such as Na_2CO_3, K_3PO_4, Cs_2CO_3, or *t*-BuOK, or another mixture known to those skilled in the art. Finally, compound 5 is transformed in one ore several synthetic steps to compound of formula (I) of the present invention. These transformations include, if necessary, the changing of the precursor groups Ar and/or R to R^2, R^3, R^4, and/or R^5 as defined in formula (I) and/or the changing of the precursor groups X', Y', Z', and/or R' to X, Y, Z, and/or R^1, respectively, as defined in formula (I). A precursor group may also be changed to a different such group. An exemplary transformation is the hydrolysis of an ester to an acid (*e.g.* Y' = -COOalkyl to Y' = -COOH). Other examples of methods used in the transformations comprise substitutions, reductions, oxidations, alkylations, esterifications, and etherifications. The precursor groups can be changed to a different such group, or to the groups defined in formula (I), at any time during the reaction sequence.

Scheme 1.



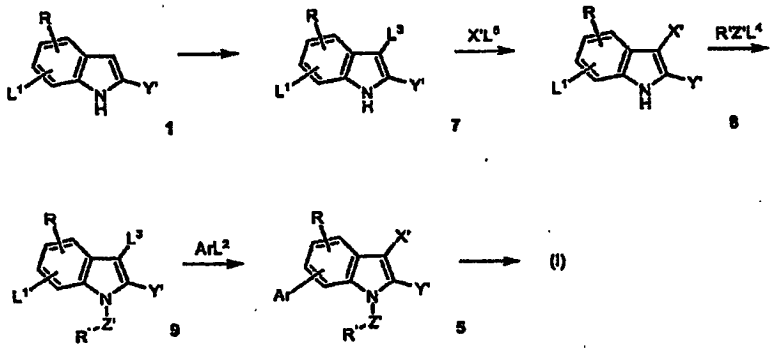
It is also understood that the various groups that are introduced onto the indole nucleus not necessarily need to be added in the order described in Scheme 1. Thus, Scheme 2 depicts a route where the substituent in the 3-position of the indole is introduced before the 1-substituent. The synthetic procedures are the same as described before. Also as previously described, the precursor groups can be changed to a different such group, or to the groups defined in formula (I), at any time during the reaction sequence.

Scheme 2.



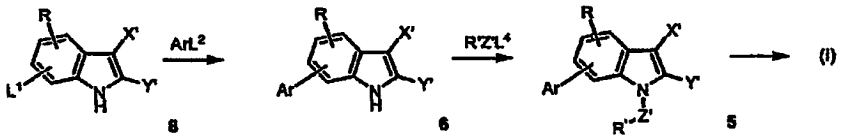
Scheme 3 describes a synthesis in which the substituent in the indolic 3-position is introduced first, followed by the substituents in the 1-position. The aromatic residue in 4-, 5-, 6-, or the 7-position is introduced last. The synthetic procedures are the same as described before. Also as previously described, the precursor groups can be changed to a different such group, or to the groups defined in formula (I), at any time during the reaction sequence.

Scheme 3.



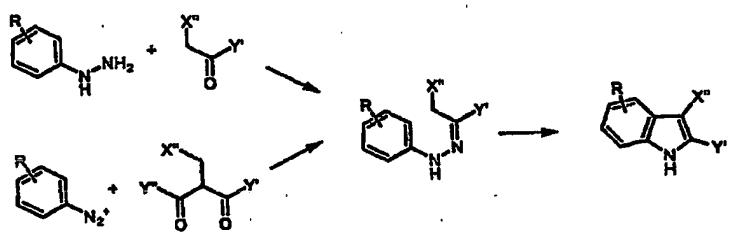
Another reaction sequence is described in Scheme 4. The synthetic procedures are the same as described before. Also as previously described, the precursor groups can be changed to a different such group, or to the groups defined in formula (I), at any time during the reaction sequence.

Scheme 4.



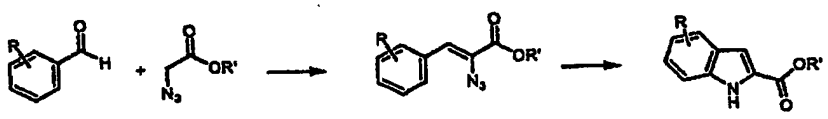
Compound 1 which is the starting material in the sequences described in Schemes 1 to 4, are either commercially available or synthesized by routes known to those skilled in the art. One such reaction is the Fischer indole synthesis (Scheme 5). This reaction can be used for the synthesis of indoles unsubstituted in their 3-positions (X'' = H) or compounds where there is a substituent in the indolic 3-position, such as compounds **6** and **8** (X'' = X'), and for certain compounds covered by structure **5** (*i.e.* when the indole nitrogen is alkylated, but not acylated). The intermediate in the Fischer indole synthesis is a hydrazone which preferably is prepared from the corresponding ketone and an appropriately substituted phenyl hydrazine, or by the Japp-Klingemann reaction, from an appropriately substituted phenyldiazonium salt and a malonic acid derivative (Y'' is –COOH or –COOalkyl) or a β-ketoester (Y'' is -C(O)alkyl).

Scheme 5.



Another useful route to appropriately substituted indolic intermediates is the Hemetsberger synthesis, which is well known to those skilled in the art (Scheme 6). The reaction is based on the condensation of an appropriately substituted benzaldehyde with an azidoacetic acid ester, followed by a thermally induced cyclization.

Scheme 6.

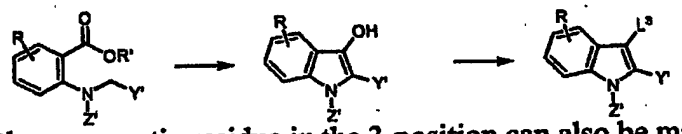


There are numerous alternative procedures for the synthesis of appropriately substituted indolic intermediates. For example, the precursor group Y', or the residue Y defined as above, can be introduced into an indolic compound unsubstituted in the 2-position. Those synthetic procedures are well known to those skilled in the art.

Yet another route to indoles, known to those skilled in the art, with a useful group in the 3-position, is depicted in Scheme 7. The scheme describes a reaction where an appropriately substituted anthranilic acid derivative is made to undergo an intramolecular condensation. The hydroxy group in the indolic 3-position is converted by methods known to those skilled in the art to a leaving group (*e.g.* to a triflate), which can be substituted by an aromatic, or an amide residue as described before. Also, reductive amination of the 3-hydroxy indole (which is the tautomer of an indoxyl) gives a compound where L^3 is an amine. Z' in the compounds of Scheme 7 is either hydrogen, protective groups,

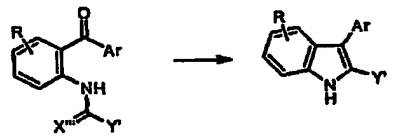
precursor groups or groups which belong to the compounds described by formula (I) of the present invention.

Scheme 7.



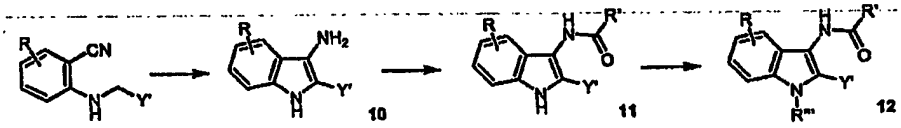
An indole with an aromatic residue in the 3-position can also be made directly by an intramolecular condensation or intramolecular reductive coupling of an appropriately substituted 2-aminobenzophenone intermediate (Scheme 8). When X''' is H/H the reaction is a base induced condensation. When X''' is O the cyclization is induced by $TiCl_3/C_8K$, $TiCl_4/Zn$, SmI_2 or similar reagents known to those skilled in the art.

Scheme 8.



Indoles with a 3-amino group can be made by an intramolecular condensation of an appropriately substituted anthralinonitrile (Scheme 9). The amino group in compound **10** can then be acylated, by methods known to those skilled in the art, to give **11**. Alkylation or acylation on the indole nitrogen, by methods known to those skilled in the art, finally gives structure **12**.

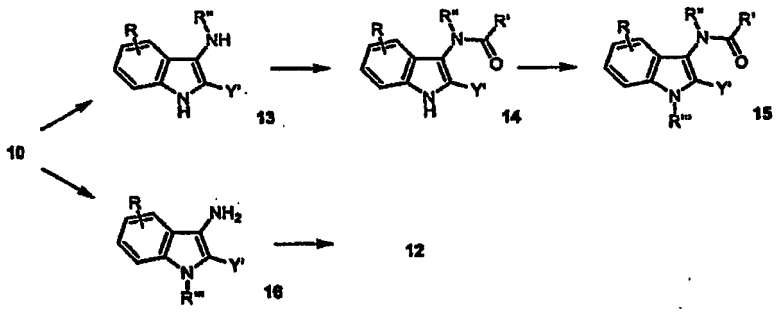
Scheme 9.



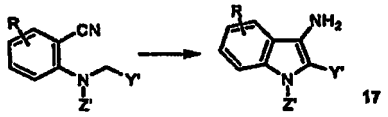
Alternative routes to the one described in Scheme 9 is depicted in Scheme 10. Alkylation of compound **10** gives **13** which can be acylated to **14** which in turn

is alkylated or acylated to afford **15**. Compound **10** can also be alkylated or acylated on the indole nitrogen to afford compound **16** which finally is converted to **12**. Yet another variation is depicted in Scheme 11. In this case the amino group in the anthranilonitrile carries a group, Z', that can be either a protective group, precursor group or group which belongs to the compounds described by formula (I) of the present invention. If the Z' group in **17** is a protective group it can be removed, by methods known to those skilled in the art, which affords compound **10**. The 3-amino group in the indole **17** may be alkylated or acylated as described above.

Scheme 10.



Scheme 11.



It is also understood that 3-amino residues can be introduced in 3-unsubstituted indoles by methods known to those skilled in the art, *e.g.* by nitration followed by reduction. Rearrangements of *e.g.* indole-3-carboxamides could also furnish 3-aminoindoles or derivatives thereof.

As explained before, the precursor groups R, R', R", R"', X", Y' and Z', in Schemes 5 to 10 may at any time during the reaction sequence be changed to a different such group, or to a corresponding group defined in formula (I).

Those skilled in the art will readily understand that known variations of the processes described herein and of the experimental conditions, such as solvents, temperatures and times, of the following preparative procedures, can be used to prepare compounds of formula (I) of the present invention.

The present invention will now be described with reference to the following Examples. These Examples are not to be regarded as limiting of the scope of the present invention, but shall only serve in an illustrative manner.

EXAMPLES

The following abbreviations are used in the examples:

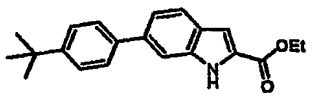
DMAP	4-dimethylaminopyridine
DMF	dimethylformamide
DMSO	dimethylsulfoxide
EtOAc	ethyl acetate
HPLC	High Pressure Liquid Chromatography
MeCN	acetonitrile
MS	Mass spectrum
NMR	Nuclear Magnetic Resonance
TFA	trifluoroacetic acid
THF	tetrahydrofuran

Chemicals specified in the synthesis of the compounds in the examples were commercially available from, *e.g.* Sigma-Aldrich Fine Chemicals or prepared according to known literature procedures.

Example 1. 6-(4-*tert*-Butylphenyl)-1-(3-phenoxybenzyl)-3-phenylindole-2-carboxylic acid (E1).

Step 1.

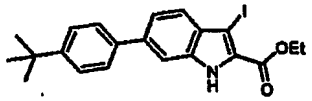
6-(4-*tert*-Butylphenyl)indole-2-carboxylic acid ethyl ester.



A mixture of 6-bromoindole-2-carboxylic acid ethyl ester (400 mg, 1.5 mmol), 4-*tert*-butylphenylboronic acid (400 mg, 2.25 mmol), K_3PO_4 (950 mg, 1.5 mmol), $Pd(OAc)_2$ (18 mg, 0.075 mmol), 2,2'-bis(di-*tert*-butylphosphino)-1,1'-biphenyl (45 mg, 0.15 mmol), and toluene (9 mL) was stirred in an argon atmosphere for 30 min at room temperature, and at 100 °C for 40 min using micro-wave irradiaton. The mixture was cooled to room temperature and poured into $NaHCO_3$ (aq., sat, 20 mL). The mixture was extracted with EtOAc (3x20 mL) and the combined extracts were washed with water (60 mL), brine (60 mL) and dried over Na_2SO_4. Concentration and purification by chromatograpy gave the title compound (392 mg, 81%).

Step 2.

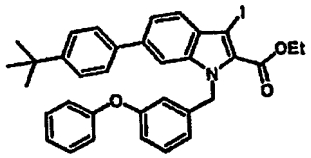
6-(4-*tert*-Butylphenyl)-3-iodoindole-2-carboxylic acid ethyl ester.



The reaction was performed with the exclusion of light. A solution of NaI (300 mg, 2.0 mmol) in acetone (15 mL) was added dropwise to a stirred solution of *N*-chlorosuccinimide (270 mg, 2.0 mmol) in acetone (4 mL), followed after 15 min by the dropwise addition of 6-(4-*tert*-butylphenyl)indole-2-carboxylic acid ethyl ester (650 mg, 2.0 mmol) in acetone (20 mL). After 30 min at room temperature the mixture was poured into an aqueous solution of $Na_2S_2O_3$ (10%, 40 ml) and extracted with EtOAc (3x50 mL). The combined extracts were washed with water (100 mL), brine (75 mL) and dried over

Na_2SO_4. Concentration and purification by chromatograpy gave the title compound (743 mg, 82%) as a brownish solid that was used without any further purification.

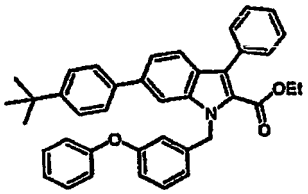
Step 3.
6-(4-*tert*-Butylphenyl)-3-iodo-1-(3-phenoxybenzyl)-indole-2-carboxylic acid ethyl ester.



A solution of 6-(4-*tert*-butylphenyl)-3-iodoindole-2-carboxylic acid ethyl ester (743 mg, 1.66 mmol) in DMF (10 mL) was added carefully to a stirred suspension of NaH (41 mg, 1.69 mmol) in DMF (4 mL) at 0 °C and the mixture was stirred at room temperature for 25 min. A solution of 3-phenoxybenzyl-chloride (378 mg, 1.69 mmol) in DMF (6 mL) was added in portions and the mixture was stirred at room temperature for 24 h, poured into water (40 mL) and extracted with *t*-BuOMe (3x50 mL). The combined extracts were washed with water (100 mL), brine (100 mL) and dried over Na_2SO_4. Concentration, chromatography and crystallization from EtOH gave the title compound (766 mg, 73%).

Step 4.

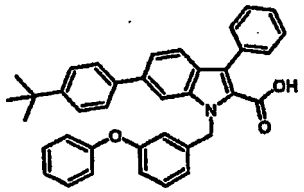
6-(4-*tert*-Butylphenyl)-1-(3-phenoxybenzyl)-3-phenylindole-2-carboxylic acid ethyl ester.



A mixture of 6-(4-*tert*-butylphenyl)-3-iodo-1-(3-phenoxybenzyl)-indole-2-carboxylic acid ethyl ester (200 mg, 0.32 mmol), phenylboronic acid (59 mg, 0.48 mmol), K_3PO_4 (238 mg, 1.12 mmol), $Pd(OAc)_2$ (3.6 mg, 0.016 mmol) and toluene (3 mL) was stirred for 20 min at room temperature and for 4h at 80 °C. The mixture was poured into $NaHCO_3$ (aq., sat, 30 mL) and extracted with EtOAc (3x20 mL). The combined extracts were washed with water (30 mL), brine (25 mL) and dried over Na_2SO_4. Concentration and purification by chromatograpy gave the title compound (163 mg, 88%).

Step5.

6-(4-*tert*-Butylphenyl)-1-(3-phenoxybenzyl)-3-phenylindole-2-carboxylic acid.

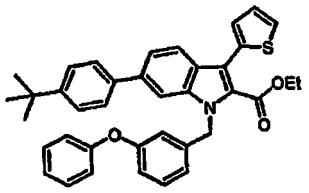


A mixture of 6-(4-*tert*-butylphenyl)-1-(3-phenoxybenzyl)-3-phenylindole-2-carboxylic acid ethyl ester (163 mg, 0.281 mmol), aqueous NaOH (1 M, 10 mL) and MeCN (40 mL) was heated at reflux for 4 h, allowed to cool, acidified with 1M HCl to pH 2 and extracted with EtOAc (3x20 mL). The combined extracts were washed with water (50 mL), brine (50 mL) and dried over Na_2SO_4. Concentration, purification by chromatograpy, and recrystallization from EtOH and from MeCN gave the title compound (95 mg, 61%). ^1H NMR (DMSO, 200 MHz): δ 7.61-7.37 (12H, m), 7.29-7.17 (3H, m), 7.09-7.00 (1H,

m), 6.97-6.90 (2H, m), 6.85 (1H, d, *J*=2.0 Hz), 6.83-6.77 (2H, m), 5.86 (2H, s), 1.37 (9H, s).

Example 2. 6-(4-*tert*-Butylphenyl)-1-(3-phenoxybenzyl)-3-(2-thienyl)indole-2-carboxylic acid (E2).

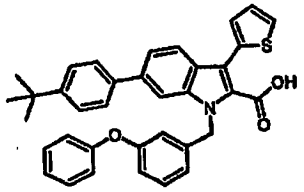
Step 1.
6-(4-*tert*-Butylphenyl)-1-(3-phenoxybenzyl)-3-(2-thienyl)indole-2-carboxylic acid ethyl ester.



2-(Tributylstannyl)thiophene (72 mg, 0.20 mmol) was added to a stirred mixture of 6-(4-*tert*-butylphenyl)-3-iodo-1-(3-phenoxybenzyl)-indole-2-carboxylic acid ethyl ester (150 mg, 0.24 mmol, prepared according to Step 4, Example 1), CuI (25 mg, 0.13 mmol), $Pd(PPh_3)_2Cl_2$ (18 mg, 0.026 mmol) and DMF (3 mL). After 10 min at room temperature and 1h at 90 °C another portion of 2-(tributylstannyl)thiophene (72 mg, 0.20 mmol) was added and the heating was continued for 3h. The mixture was filtered through Celite® and the solids were washed with EtOAc (100 mL). Concentration and purification by chromatograpy gave the title compound (125 mg, 90%).

Step 2.

6-(4-*tert*-Butylphenyl)-1-(3-phenoxybenzyl)-3-(2-thienyl)indole-2-carboxylic acid ethyl ester.

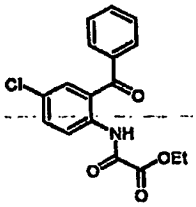


A mixture of 6-(4-*tert*-butylphenyl)-1-(3-phenoxybenzyl)-3-phenylindole-2-carboxylic acid ethyl ester (125 mg, 0.213 mmol), aqueous KOH (2 M, 2 mL) and MeCN (6 mL) was heated using micro-wave irradiation for 30 min at 130 °C. The mixture was acidified with 1M HCl to pH 2 and extracted with EtOAc (4x20 mL). The combined extracts were washed with water (50 mL), brine (50 mL) and dried over Na_2SO_4. Concentration and purification by chromatograpy gave the title compound (91 mg, 77%). ^{1}H NMR (DMSO, 200 MHz): δ 7.75 (1H, d, *J*=8.4 Hz), 7.56-7.45 (6H, m), 7.44 (1H, dd, *J*=4.0, 1.4 Hz), 7.30-7.15 (5H, m), 7.09-7.03 (1H, m), 6.98-6.90 (2H, m), 6.86-6.79 (3H, m), 5.86 (2H, s), 1.37 (9H, s).

Example 3. 5-(3,4-methylenedioxyphenyl)-3-phenyl-1-(3-phenylpropyl)indole-2-carboxylic acid (E3).

Step 1.

N-(2-Benzoyl-4-chlorophenyl)oxalamic acid ethyl ester.

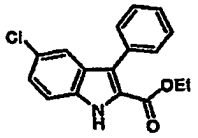


A mixture of 2-amino-5-chlorobenzophenone (11.6 g, 50 mmol), ethyl oxalyl-chloride (6.8 g, 50 mmol) and toluene (70 mL) was heated at reflux for 1.5 h. On cooling a yellow precipitate formed. EtOAc (250 mL) was added and the solution

was washed with $NaHCO_3$ (5%, 100 ml), H_3PO_4 (5%, 100 ml), brine (100 mL) and dried over Na_2SO_4. Concentration gave the title compound (15.5g, 94%).

Step 2.

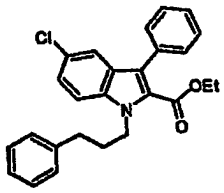
5-Chloro-3-phenylindole-2-carboxylic acid ethyl ester.



$TiCl_4$ in THF (0.25 M, 19.5 mL, 54.9 mmol) was added slowly to a stirred mixture of *N*-(2-benzoyl-4-chlorophenyl)oxalamic acid ethyl ester (8.88 g, 26.8 mmol), Zn (7.19 g, 110 mmol) and THF (60 mL) at room temperature. After 2h silica gel was added and after another 30 min the mixture was filtered through a pad of silica gel which was washed with EtOAc (300 mL). The combined filtrates were washed with $NaHCO_3$ (5%, 300 ml), water (300 ml), brine (100 mL) and dried over Na_2SO_4. Concentration and crystallization of the residue from CH_2Cl_2 and petroleum ether gave the title compound (3.13g, 39%).

Step 3.

5-Chloro-3-phenyl-1-(3-phenylpropyl)indole-2-carboxylic acid ethyl ester.

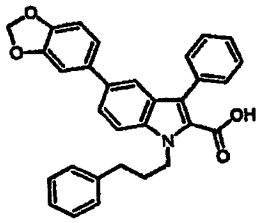


NaH (60 % dispersion in mineral oil, 0.25 g, 6.2 mmol) was washed with hexane (2x1mL) and Et_2O (1 mL) and suspended in DMF (1 mL). A solution of 5-chloro-3-phenylindole-2-carboxylic acid ethyl ester (1.55 g, 5.17 mmol) in DMF (10 mL) was added carefully at 0 °C and the mixture was stirred for 20 min. A solution of (3-bromopropyl)-benzene (1.54 g, 7.75 mmol) in DMF (3mL) was added carefully at 0 °C. The cooling bath was removed and the mixture was stirred at room temperature for 16 h, poured into water (200 mL), and extracted with EtOAc (150 mL). The extract was washed with water (2x50

mL), brine (150 mL) and dried over Na_2SO_4. Concentration and chromatography gave the title compound (1.66 g, 77%).

Step 4.

5-(3,4-Methylenedioxyphenyl)-3-phenyl-1-(3-phenylpropyl)indole-2-carboxylic acid.

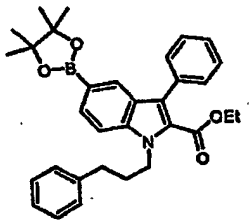


The title compound was prepared according to the procedure in Example 1, Step 1, from 5-chloro-3-phenyl-1-(3-phenylpropyl)indole-2-carboxylic acid ethyl ester and 3,4-methylenedioxyphenylboronic acid, followed by hydrolysis according to Example 2, Step 2. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.61-7.38 (8H, m), 7.36-7.15 (5H, m), 7.04 (1H, s), 7.02 (1H, dd, *J*=8.5, 1.8 Hz), 6.85 (1H, d, *J*=8.5 Hz), 5.98 (2H, s), 4.67-4.55 (2H, m), 2.75 (2H, t, *J*=7.6 Hz), 2.31-2.12 (2H, m).

Example 4. 3-Phenyl-1-(3-phenylpropyl)-5-(3-pyridinyl)indole-2-carboxylic acid (E4).

Step 1.

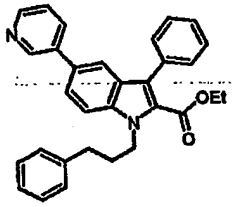
3-Phenyl-1-(3-phenylpropyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-indole-2-carboxylic acid ethyl ester.



A 0.01 M stock solution of a $Pd/(C_6H_{11})_3P$ was prepared from Pd_2dba_3, (0.457 g, 0.5 mmol), tricyclohexylphosphine (0.841 g, 3 mmol) and dioxane (100 mL). An aliquot of this stock solution (12.5 mL, 0.125 mmol Pd), 5-chloro-3-phenyl-1-(3-phenylpropyl)indole-2-carboxylic acid ethyl ester (1.05 g, 2.5 mmol) prepared according to Example 3, Step 3, bis(pinacolato)diboron (0.762 g, 3.0 mmol), KOAc (0.44 g, 4.5 mmol), and dioxane (25 mL) was heated at 80 °C for 16 h. Another aliquot of the $Pd/(C_6H_{11})_3P$ reagent (2.5 mL, 0.025 mmol Pd) was added and the mixture was heated at 100 °C for 24 h. The mixture was filtered through Celite®, and the filtrate was concentrated and purified by chromatography to give the title compound (0.47 g, 37 %) together with 0.55 g recovered starting material.

Step 2.

3-Phenyl-1-(3-phenylpropyl)-5-(3-pyridinyl)indole-2-carboxylic acid ethyl ester.

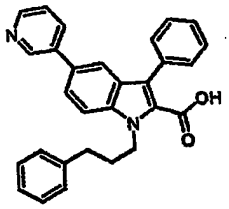


3-Phenyl-1-(3-phenylpropyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-indole-2-carboxylic acid ethyl ester (0.40 g, 91 mmol), 3-iodopyridine (0.28 g,

1.37 mmol), aqueous Na_2CO_3 (2M, 0.46 mL, 0.91 mmol), $Pd(PPh_3)_4$ (53 mg, 46 μmol), toluene (7.3 mL), and EtOH (1.8 mL) was heated at 80 °C for 16 h. More 3-iodopyridine(0.19 g, 0.91 mmol), aqueous Na_2CO_3 (2M, 1.4 mL, 2.73 mmol), and $Pd(PPh_3)_4$ (23 mg, 20 μmol) were added and the mixture was heated for another 8h. EtOAc (30 mL) and brine (30 mL) were added. The layers were separated and the aqueous phase was washed with EtOAc (30 mL). The combined organic phases were dried with brine (30 mL) and Na_2SO_4. Concentration and chromatography gave the title compound (0.32 g, 76%).

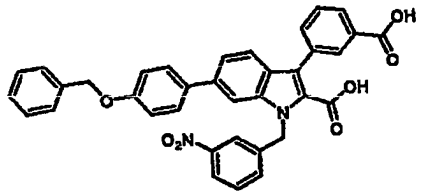
Step 3.

3-Phenyl-1-(3-phenylpropyl)-5-(3-pyridinyl)indole-2-carboxylic acid



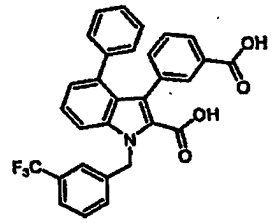
The title compound was prepared from 3-phenyl-1-(3-phenylpropyl)-5-(3-pyridinyl)indole-2-carboxylic acid ethyl ester according to the procedure in Example 2, Step 2. ^1H NMR ($CDCl_3$, 200 MHz): δ 8.78 (1H, s), 8.52 (1H, d, *J*=4.2 Hz), 7.92 (1H, d, *J*=8.0 Hz)), 7.65-7.71 (1H, m), 7.59-7.13 (13H, m), 4.71-4.58 (2H, m), 2.75 (2H, t, *J*=7.6 Hz), 2.32-2.17 (2H, m).

Example 5. 6-(4-Benzyloxyphenyl)-3-(3-carboxyphenyl)-1-(3-nitrobenzyl)-indole-2-carboxylic acid (E5).



The title compound was prepared according to the procedure in Example 1 from 4-benzyloxyphenylboronic acid, 3-nitrobenzylbromide and 3-carboxyphenylboronic acid. ^{1}H NMR (DMSO, 200 MHz): δ 13.02 (2H, s), 8.13-7.94 (5H, m), 7.75 (1H, ddd, *J*=7.6, 1.5, 1.5 Hz), 7.63 (1H, dd, *J*=7.6, 2.0 Hz), 7.59-7.27 (12H, m), 7.04-6.97 (1H, m), 6.12 (2H, s), 5.18 (2H, s).

Example 6. 3-(3-Carboxyphenyl)-4-phenyl-1-(3-trifluoromethylbenzyl)indole-2-carboxylic acid (E6).

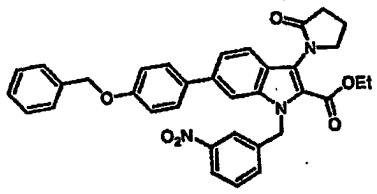


The title compound was prepared according to the procedure in Example 1 from 4-bromoindole-2-carboxylic acid ethyl ester, phenylboronic acid, 3-trifluoromethylbenzylbromide and 3-carboxyphenylboronic acid. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.79 (1H, dd, *J*=1.5, 1.5 Hz), 7.70 (1H, ddd, *J*=7.7, 1.5, 1.5 Hz), 7.57-7.50 (2H, m), 7.47-7.34 (3H, m), 7.25-7.20 (1H, m), 7.06 (1H, dd, *J*=6.2, 1.8 Hz), 7.06-6.85 (7H, m), 5.93 (2H, s).

Example 7. 6-(4-Benzyloxyphenyl)-1-(3-nitrobenzyl)-3-(2-oxopyrrolidin-1-yl)-indole-2-carboxylic acid (E7).

Step 1.

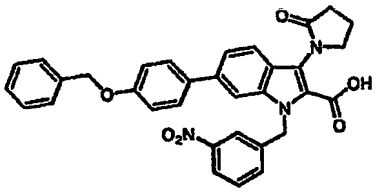
6-(4-Benzyloxyphenyl)-1-(3-nitrobenzyl)-3-(2-oxopyrrolidin-1-yl)indole-2-carboxylic acid ethyl ester.



A stock suspension of a CuI/$MeNHCH_2CH_2NHMe$ complex was prepared by heating CuI (95.2 mg, 0.5 mmol), $MeNHCH_2CH_2NHMe$ (213μL, 2.0 mml), and dioxane (5 mL) at 100 °C for 5 min using micro-wave irridiation. 1.5 mL of this solution was added to 6-(4-benzyloxyphenyl)-3-iodo-1-(3-nitrobenzyl)indole-2-carboxylic acid ethyl ester (630 mg, 1.0 mmol, prepared according to the procedure in Example 1 from 6-bromoindole-2-carboxylic acid ethyl ester, 4-benzyloxyphenylboronic acid, and 3-nitrobenzylbromide), K_3PO_4 (530 mg, 2.5 mmol), and dioxane (5 mL). Pyrrolidone (390 mg, 5.0 mmol) was added and the mixture was stirred at 95 °C for 24 h, cooled to room-temperature, pored into aqueous HCl (0.1 M, 100 mL) and extracted with EtOAc (4x15 mL). The combined extracts were dried with brine (30 mL) and Na_2SO_4. Concentration and chromatography gave the title compound (538 mg, 91%).

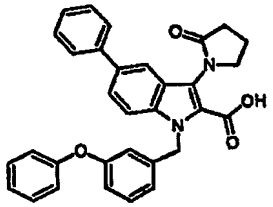
Step 2.

6-(4-Benzyloxyphenyl)-1-(3-nitrobenzyl)-3-(2-oxopyrrolidin-1-yl)indole-2-carboxylic acid.



6-(4-Benzyloxyphenyl)-1-(3-nitrobenzyl)-3-(2-oxopyrrolidin-1-yl)indole-2-carboxylic acid ethyl ester was hydrolyzed in anology with Example 2, Step 2, using dioxane as the solvent, to give the title compound. ^{1}H NMR (DMSO, 200 MHz): δ 13.37 (1H, s), 8.10-8.06 (2H, m), 7.96 (1H, s), 7.66-7.26 (12H, m), 7.00 (1H, d, *J*=7.8 Hz), 6.06 (2H, s), 5.17 (2H, s), 3.81-3.74 (2H, m), 2.46-2.38 (2H, m), 2.24-2.06 (2H, m).

Example 8. 3-(2-Oxopyrrolidin-1-yl)-1-(3-phenoxybenzyl)-5-phenylindole-2-carboxylic acid (E8).

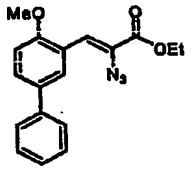


The title compound was prepared according to the procedure in Example 7 from 5-bromoindole-2-carboxylic acid ethyl ester, phenylboronic acid, 3-phenoxybenzylchloride and pyrrolidone. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.69-7.65 (1H, m), 7.63-7.52 (3H, m), 7.50-7.15 (7H, m), 7.13-7.01 (1H, m), 7.00-6.91 (2H, m), 6.88-6.79 (3H, m), 5.74 (2H, s), 3.98 (2H, t, *J*=7.0 Hz), 2.72 (2H, t, *J*=8.0 Hz), 2.41-2.34 (2H, m).

Example 9. 1-(3,5-Difluorobenzyl)-4-methoxy-3-(2-oxopyrrolidin-1-yl)-7-phenylindole-2-carboxylic acid (E9).

Step 1.

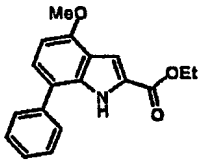
2-Azido-3-(4-methoxybiphenyl-3-yl)acrylic acid ethyl ester.



A solution of 4-methoxybiphenyl-3-carbaldehyde (1.8 g, 8.48 mmol) and azidoacetic acid ethyl ester (5.62 g, 44 mmol) in EtOH (15 mL) was added dropwise to a solution of NaOEt (3.13 g, 46 mmol) in EtOH (35 mL) at -25 °C. The mixture was stirred at that temperature for 10 min, kept in the freezer (-18 °C) for 24 h and poured with vigourous stirring to a cooled (0 °C) saturated aquous solution of NH_4Cl (200 mL). The mixture was extracted with EtOAc (3x25 mL) and the combined extracts were washed with brine (50 mL) and dried over Na_2SO_4. Concentration and crystallization from EtOH gave the title compound (1.80 g, 66%).

Step 2.

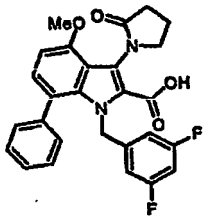
4-Methoxy-7-phenylindol-2-carboxylic acid ethyl ester.



A solution of 2-azido-3-(4-methoxybiphenyl-3-yl)acrylic acid ethyl ester (1.75 g, 5.40 mmol) in *o*-xylene (25 mL) was added dropwise to boiling *o*-xylene (25 mL). The heating was continued for 5 min and the solution was allowed to cool to room temperature and kept in the freezer (-18 °C) for 16 h. The title compound precipitated and was filtered off, washed with petroleum ether and dried *in vacuo* (1.20 g, 74%).

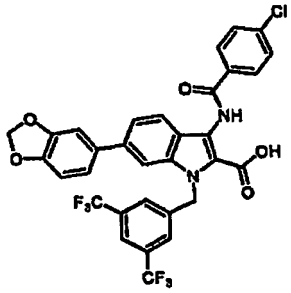
Step 3.

1-(3,5-Difluorobenzyl)-4-methoxy-3-(2-oxopyrrolidin-1-yl)-7-phenylindole-2-carboxylic acid



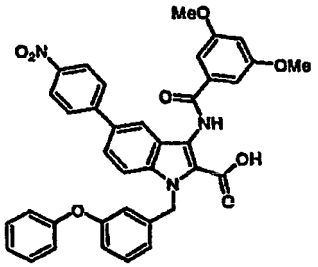
The title compound was prepared from 4-methoxy-7-phenylindole-2-carboxylic acid ethyl ester following the procedure in Example 7. ^{1}H NMR (DMSO, 200 MHz): δ 7.34-7.21 (3H, m), 7.10-7.06 (2H, m), 7.01-6.91 (1H, m), 6.94 (1H, d, *J*=7.8 Hz), 6.67 (1H, d, *J*=8.1 Hz), 5.92-5.89 (2H, m), 5.51-5.28 (2H, m), 3.89 (3H, s), 3.77-3.67 (2H, m), 2.37-2.17 (2H, m), 2.14-2.10 (2H, m).

Example 10. 6-(3,4-Methylenedioxyphenyl)-1-(3,5-bis-trifluoromethylbenzyl)-3-(4-chlorobenzoylamino)indole-2-carboxylic acid (E10).



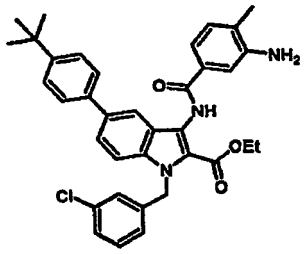
The title compound was prepared according to the procedure in Example 7 from 6-bromoindole-2-carboxylic acid ethyl ester, 3,4-methylenedioxyphenylboronic acid, 3,5-bis-trifluoromethylbenzylchloride and 4-chlorobenzamide. ^{1}H NMR (DMSO, 200 MHz): δ 10.35 (1H, s), 8.09-8.03 (2H, m), 8.01-7.99 (1H, m), 7.95-7.94 (1H, m), 7.81 (2H, s), 7.73 (1H, d, *J*=8.6 Hz), 7.66-7.59 (2H, m), 7.44 (1H, dd, *J*=8.6, 1.2 Hz), 7.34 (1H, d, *J*=1.8 Hz), 7.22 (1H, dd, *J*=8.2, 1.8 Hz), 6.99 (1H, d, *J*=8.2 Hz), 6.08 (2H, s), 6.05 (2H, s).

Example 11. 3-(3,5-Dimethoxybenzoylamino)-5-(4-nitrophenyl)-1-(3-phenoxy-benzyl)indole-2-carboxylic acid (E11).



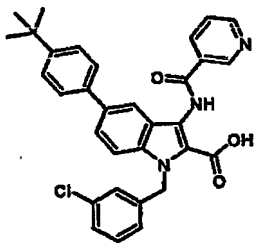
The title compound was prepared from 5-(4-nitrophenyl)indole-2-carboxylic acid ethyl ester (prepared from 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)indole-2-carboxylic acid ethyl ester (prepared from 5-bromoindole-2-carboxylic acid ethyl ester and 4-nitrobrombenzene)), 3-phenoxybenzylchloride and 3,5-dimethoxybenzamide according to the procedure in Example 7. ^{1}H NMR (DMSO, 200 MHz): δ 10.37 (1H, s), 8.32-8.24 (2H, m), 8.15 (1H, s), 8.01-7.91 (2H, m), 7.76 (2H, s), 7.41-7.16 (5H, m), 7.15-7.05 (1H, m), 6.99-6.90 (2H, m), 6.84-6.69 (4H, m), 5.90 (2H, s), 3.81 (6H, s).

Example 12. 3-(3-Amino-4-methylbenzoylamino)-5-(4-*tert*-butylphenyl)-1-(3-chlorobenzyl)indole-2-carboxylic acid (E12).



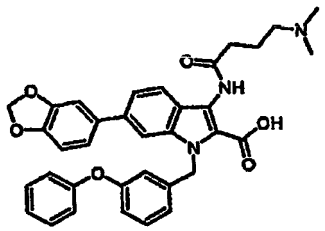
The title compound was prepared according to the procedure in Example 7 from 5-bromoindole-2-carboxylic acid ethyl ester, 4-*tert*-butylphenylboronic acid, 3-chlorobenzylchloride and 3-amino-4-methylbenzamide. ^{1}H NMR (DMSO, 200 MHz): δ 10.09 (1H, s), 8.00 (1H, s), 7.69-7.40 (6H, m), 7.36-7.31 (3H, m), 7.19-6.94 (3H, m), 5.86 (2H, s), 4.3 (1H, br s), 3.3 (1H, br s), 2.11 (3H, s), 1.29 (9H, s).

Example 13. 5-(4-*tert*-Butylphenyl)-1-(3-chlorobenzyl)-3-[(pyridine-3-carbonyl)-amino]indole-2-carboxylic acid (E13).



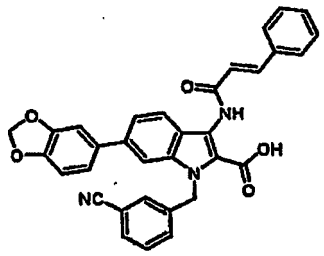
The title compound was prepared according to the procedure in Example 7 from 5-bromoindole-2-carboxylic acid ethyl ester, 4-*tert*-butylphenylboronic acid, 3-chlorobenzylchloride and nicotinamide. ^{1}H NMR (DMSO, 200 MHz): δ 10.50 (1H, s), 9.20 (1H, s), 8.80-8.71 (1H, m), 8.42-8.31 (1H, m), 7.91 (1H, s), 7.32-7.52 (5H, m), 7.48-7.40 (2H, m), 7.34-7.27 (2H, m), 7.14 (1H, s), 7.06-6.97 (1H, m), 5.89 (2H, s), 1.29 (9H, s).

Example 14. 3-(4-dimethylaminobutyrylamino)-6-(3,4-methylenedioxyphenyl)-1-(3-phenoxybenzyl)indole-2-carboxylic acid(E14).



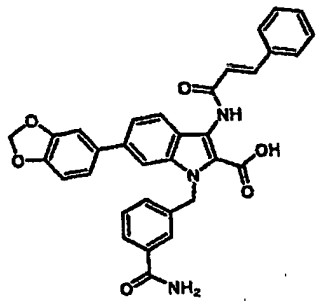
The title compound was prepared according to the procedure in Example 7 from 6-bromoindole-2-carboxylic acid ethyl ester, 3,4-methylenedioxy-phenylboronic acid, 3-phenoxybenzylchloride and 4-dimethylaminobutyramide. ^{1}H NMR (DMSO, 200 MHz): δ 12.3-11.2 (1H, br s), 8.22 (1H, d, *J*=8.6 Hz), 7.54 (1H, s), 7.37-7.05 (7H, m), 7.00-6.84 (5H, m), 6.71 (1H, dd, *J*=8.2, 2.3 Hz), 6.14 (2H, s), 6.07 (2H, s), 2.81 (2H, t, *J*=7.5 Hz), 2.54 (6H, s), 2.46 (2H, t, *J*=7.3 Hz), 1.94 (2H, dt, *J*=7.5, 7.3 Hz).

Example 15. 1-(3-Cyanobenzyl)-6-(3,4-methylenedioxyphenyl)-3-(3-phenyl-acryloylamino)indole-2-carboxylic acid (E15).



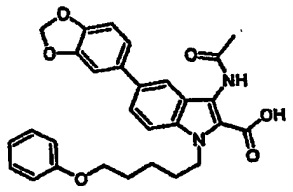
The title compound was prepared according to the procedure in Example 7 from 6-bromoindole-2-carboxylic acid ethyl ester, 3,4-methylenedioxy-phenylboronic acid, 3-cyanobenzylchloride and cinnamamide. ^{1}H NMR (DMSO, 200 MHz): δ 11.95 (1H, br s), 8.28 (1H, d, *J*=8.6 Hz), 7.70-7.59 (6H, m), 7.54-7.37 (6H, m), 7.28-7.23 (2H, m), 7.15 (1H, dd, *J*=8.2, 1.8 Hz), 6.96 (1H, d, *J*=8.2 Hz), 6.88 (1H, d, *J*=15.8 Hz), 6.16 (2H, s), 6.03 (2H, s).

Example 16. 1-(3-Carbamoylbenzyl)-6-(3,4-methylenedioxyphenyl)-3-(3-phenylacryloylamino)indole-2-carboxylic acid (E16).



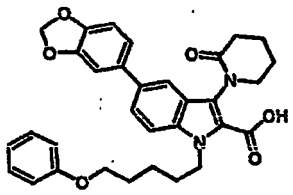
The title compound was isolated in the last synthetic step (the hydrolysis) in the preparation of the title compound of Example 15. ^{1}H NMR (DMSO, 200 MHz): δ 11.58 (1H, br s), 8.17 (1H, d, *J*=8.6 Hz), 7.89 (1H, s), 7.74-7.55 (6H, m), 7.48-7.37 (3H, m), 7.34-7.23 (4H, m), 7.16-7.08 (2H, m), 6.95 (1H, d, *J*=8.2 Hz), 6.91 (1H, d, *J*=15.6 Hz), 6.13 (2H, s), 6.03 (2H, s).

Example 17. 3-Acetylamino-5-(3,4-methylenedioxyphenyl)-1-(5-phenoxy-pentyl)indole-2-carboxylic acid (E17).



The title compound was prepared according to the procedure in Example 7 from 5-bromoindole-2-carboxylic acid ethyl ester, 3,4-methylenedioxy-phenylboronic acid, (5-bromopentyloxy)benzene, and acetamide. ^{1}H NMR (DMSO, 200 MHz): δ 9.60 (1H, s), 7.71 (1H, s), 7.65-7.49 (2H, m), 7.30-7.15 (3H, m), 7.09 (1H, dd, *J*=8.1, 1.4 Hz), 6.77 (1H, d, *J*=8.1 Hz), 6.93-6.82 (3H, m), 6.04 (2H, s), 4.60-4.46 (2H, m), 3.90 (2H, t, *J*=6.3 Hz), 2.09 (3H, s), 1.81-1.61 (4H, m), 1.48-1.32 (2H, m).

Example 18. 5-(3,4-Methylenedioxyphenyl)-3-(2-oxopiperidin-1-yl)-1-(5-phenoxypentyl)indole-2-carboxylic acid (E18).



The title compound was prepared according to the procedure in Example 7 from 5-bromoindole-2-carboxylic acid ethyl ester, 3,4-methylenedioxy-phenylboronic acid, (5-bromopentyloxy)benzene, and 2-piperidone. ^{1}H NMR (DMSO, 200 MHz): δ 7.66-7.49 (3H, m), 7.30-7.18 (3H, m), 7.13 (1H, dd, *J*=8.1, 1.8 Hz), 6.97 (1H, d, *J*=8.1 Hz), 6.92-6.83 (3H, m), 6.04 (2H, s), 4.65-4.50 (2H, m), 3.91 (2H, t, *J*=6.4 Hz), 3.64-3.55 (2H, m), 2.44-2.28 (2H, m), 1.98-1.64 (8H, m), 1.52-1.33 (2H, m).

Example 19: Preparation of pharmaceutical compositions

Ingredients		mg/tablet
1.	Active compound	10.0
2.	Cellulose, microcrystalline	57.0
3.	Calcium hydrogen phosphate	15.0
4.	Sodium starch glycolate	5.0
5.	Silicon dioxide, colloidal	0.25
6.	Magnesium stearate	0.75

The active ingredient 1 is mixed with ingredients 2, 3, 4 and 5 for about 10 minutes. The magnesium stearate is then added, and the resultant mixture is mixed for about 5 minutes and compressed into tablet form with or without film-coating.

Example 20: Enzyme assay and results.

In the assay mPGES catalyses the reaction where the substrate PGH_2 is converted to PGE_2. mPGES is expressed in *E. coli* and the membrane fraction is

dissolved in 20mM NaPi-buffer pH 8.0 and stored at -80 °C. In the assay mPGES is dissolved in 0,1M KPi-buffer pH 7,35 with 2,5mM glutathione. The stop solution consists of H_2O / MeCN (7/3), containing $FeCl_2$ (25 mM) and HCl (0.15 M). The assay is performed at room temperature in 96-well plates.

Analysis of the amount of PGE_2 is performed with reversed phase HPLC (Waters 2795 equipped with a 3.9x150 mm C18 column). The mobile phase consists of H_2O / MeCN (7/3), containing TFA (0.056%), and absorbance is measured at 195 nm with a Waters 2487 UV-detector.

The following is added chronologically to each well:

1. 100 µL mPGES in KPi-buffer with glutathione. Total protein concentration: 0.02 mg/mL.
2. 1 µL inhibitor in DMSO. Incubation of the plate at room temperature for 25 minutes.
3. 4 µL of a 0,25 mM PGH_2 solution. Incubation of the plate at room temperature for 60 seconds.
4. 100 µL stop solution.

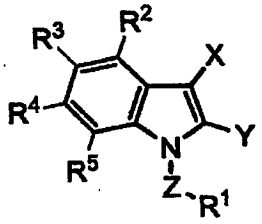
180 uL per sample is analyzed with HPLC.

The inhibition of mPGES obtained using the method described above is examplified by the compounds listed in the following table:

Example 1:	96% @10 μM
Example 2:	100% @10 μM
Example 3:	85% @10 μM
Example 8:	81% @10 μM
Example 10:	93% @10 μM
Example 12:	100% @10 μM

CLAIMS

1. A compound of formula (I):



(I)

wherein:

X is an optionally substituted aryl or heteroaryl residue, or an optionally substituted amide residue connected through its nitrogen atom;

Y is a carboxylic acid, a carboxylic acid ester, a carboxylic acid amide, a hydroxamic acid, a hydroxamic acid ester, or hydroxymethyl;

Z is a spacer;

R^1 is an optionally substituted aryl or heteroaryl residue;

At least one of R^2, R^3, R^4, or R^5 is an optionally substituted aryl or heteroaryl residue.

2. A compound according to claim 1 wherein:

X is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) $R^6C(O)N(R^7)$–;

Y is selected from $HOCH_2$–, $(R^8)NHC(O)$–, $R^8ONHC(O)$–, and $R^8OC(O)$–;

Z is a C_{1-8}-alkylene chain or a heteroalkylene chain having 2 to 8 chain atoms, which optionally contains one or more unsaturations, wherein the C_{1-8}-alkylene chain and the heteroalkylene chain may be optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, and O=; and wherein one or more atoms of the C_{1-8}-alkylene chain or the heteroalkylene chain are optionally part of an additional C_{3-8}-cycloalkyl-, or C_{3-8}-heterocycloalkyl-ring, where the said ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and optionally is substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, and O=;

R^1 is selected from aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

R^2, R^3, R^4, and R^5 are each independently selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

(iii) hydrogen, halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

or any adjacent pair of R^2, R^3, R^4, or R^5 may be part of an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

provided that at least one of R^2, R^3, R^4, or R^5 is aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

A is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

(iii) halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

B is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, and by an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is

optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

(iii) halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene

chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

R^6 and R^7 are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

or where R^6 and R^7 are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–,

$R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

R^8, R^9, R^{10}, R^{11}, and R^{12} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(W)$–, $(R^{14})(R^{15})NC(W)$–, $R^{13}OC(W)$–, $R^{13}SC(W)$–, $(R^{14})(R^{15})N$–, $R^{13}C(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})C(W')N(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})$–, $R^{13}SC(W)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})S(O)_qN(R^{17})$–, $R^{13}OC(W)N(R^{16})S(O)_qN(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})S(O)_qN(R^{17})$–, $R^{13}OS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(W)O$–, $(R^{14})(R^{15})NC(W)O$–, $R^{13}OC(W)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, and by an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^{13}–, $R^{13}O$–, and O=;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(W)$–, $(R^{14})(R^{15})NC(W)$–, $R^{13}OC(W)$–, $R^{13}SC(W)$–, $(R^{14})(R^{15})N$–, $R^{13}C(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})C(W')N(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})$–, $R^{13}SC(W)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})S(O)_qN(R^{17})$–, $R^{13}OC(W)N(R^{16})S(O)_qN(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})S(O)_qN(R^{17})$–, $R^{13}OS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(W)O$–, $(R^{14})(R^{15})NC(W)O$–, $R^{13}OC(W)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, S=, $R^{13}N$=, $(R^{14})(R^{15})NN$=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^{14})(R^{15})C$=;

or where any pair of R^8, R^9, R^{10}, R^{11}, and R^{12} are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{13}–, $R^{13}C(W)$–, $(R^{14})(R^{15})NC(W)$–, $R^{13}OC(W)$–, $R^{13}SC(W)$–, $(R^{14})(R^{15})N$–, $R^{13}C(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})C(W')N(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})C(W')N(R^{17})$–, $R^{13}OC(W)N(R^{16})$–, $R^{13}SC(W)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $(R^{14})(R^{15})NC(W)N(R^{16})S(O)_qN(R^{17})$–, $R^{13}OC(W)N(R^{16})S(O)_qN(R^{17})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})S(O)_qN(R^{17})$–, $R^{13}OS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(W)O$–, $(R^{14})(R^{15})NC(W)O$–, $R^{13}OC(W)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, S=, $R^{13}N$=, $(R^{14})(R^{15})NN$=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^{14})(R^{15})C$=;

R^{13}, R^{14}, R^{15}, R^{16} and R^{17} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $R^{18}SC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})C(O)N(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})$–, $R^{18}SC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})S(O)_qN(R^{22})$–, $R^{18}OC(O)N(R^{21})S(O)_qN(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})S(O)_qN(R^{22})$–, $R^{18}OS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–, $R^{18}OS(O)_qO$–, $R^{18}S$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $R^{18}SC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})C(O)N(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})$–, $R^{18}SC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})S(O)_qN(R^{22})$–, $R^{18}OC(O)N(R^{21})S(O)_qN(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})S(O)_qN(R^{22})$–, $R^{18}OS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–, $R^{18}OS(O)_qO$–, $R^{18}S$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, O=, S=, $R^{18}N$=, $(R^{19})(R^{20})NN$=, $R^{18}ON$=, $(R^{19})(R^{20})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^{19})(R^{20})C$=;

or where any pair of R^{13}, R^{14}, R^{15}, R^{16} and R^{17} are optionally joined to form a 5-7 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $R^{18}SC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})C(O)N(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})C(O)N(R^{22})$–, $R^{18}OC(O)N(R^{21})$–, $R^{18}SC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})S(O)_qN(R^{22})$–, $R^{18}OC(O)N(R^{21})S(O)_qN(R^{22})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})S(O)_qN(R^{22})$–, $R^{18}OS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–, $R^{18}OS(O)_qO$–, $R^{18}S$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, O=, S=, $R^{18}N$=, $(R^{19})(R^{20})NN$=, $R^{18}ON$=, $(R^{19})(R^{20})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^{19})(R^{20})C$=;

R^{18}, R^{19}, R^{20}, R^{21} and R^{22} are each independently selected from:

(i) hydrogen;

(ii) C_{1-6}-alkyl, optionally substituted in one or more positions by one or more halogens, H_2N–, MeHN–, EtHN–, *i*-PrHN–, Me_2N–, Et(Me)N–, *i*-Pr(Me)N–, Et_2N–, HO–, MeO–, EtO–, *i*-PrO– or =O;

Q and Q' are substituents connected by a double bond, and are each independently selected from:

O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

W and W' are substituents connected by a double bond, and are each independently selected from:

O=, S=, $R^{13}N$=, $(R^{14})(R^{15})NN$=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^{14})(R^{15})C$=;

q is 1 or 2;

as well as pharmaceutically acceptable salts, stereoisomers or prodrugs thereof.

3. A compound according to claim 2 wherein:

X is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) $R^6C(O)N(R^7)$–;

Y is selected from $(R^8)NHC(O)$–, $R^8ONHC(O)$–, and $R^8OC(O)$–;

Z is a C_{1-8}-alkylene chain or a heteroalkylene chain having 2 to 8 chain atoms, which optionally contains one or more unsaturations, wherein the C_{1-8}-alkylene chain and the heteroalkylene chain may be optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, and O=; and wherein one or more atoms of the C_{1-8}-alkylene chain or the heteroalkylene chain are optionally part of an additional C_{3-8}-cycloalkyl-, or C_{3-8}-heterocycloalkyl-ring, where the said ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and optionally is substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, and O=;

R^1 is selected from aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

R^2, R^3, R^4, and R^5 are each independently selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

(iii) hydrogen, halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

or any adjacent pair of R^2, R^3, R^4, or R^5 may be part of an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms, where the alkylene or heteroalkylene chain is optionally substituted in one or

more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

provided that at least one of R^2, R^3, R^4, or R^5 is aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

A is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

(iii) halogen, NC–, R^8–, $R^8C(Q)$–, $(R^9)(R^{10})NC(Q)$–, $R^8OC(Q)$–, $R^8SC(Q)$–, $(R^9)(R^{10})N$–, $R^8C(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})C(Q')N(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})C(Q')N(R^{12})$–, $R^8OC(Q)N(R^{11})$–, $R^8SC(Q)N(R^{11})$–, N_3–,

O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, $(R^9)(R^{10})NC(Q)N(R^{11})S(O)_qN(R^{12})$–, $R^8OC(Q)N(R^{11})S(O)_qN(R^{12})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})S(O)_qN(R^{12})$–, $R^8OS(O)_qN(R^{11})$–, R^8O–, $R^8C(Q)O$–, $(R^9)(R^{10})NC(Q)O$–, $R^8OC(Q)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, R^8S–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

B is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, and by an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–,

$R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, or O=;

R^6 and R^7 are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B,

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–,

R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

or where R^6 and R^7 are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

R^8, R^9, R^{10}, R^{11}, and R^{12} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–,$(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, and by an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^{13}–, $R^{13}O$–, and O=;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-hetero-cycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, $(R^{14})(R^{15})NN$=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

or where any pair of R^8, R^9, R^{10}, R^{11}, and R^{12} are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, $(R^{14})(R^{15})NN$=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

R^{13}, R^{14}, R^{15}, and R^{16} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $R^{18}OC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–,

$(R^{19})(R^{20})NS(O)_qO-$, $R^{18}OS(O)_qO-$, $R^{18}S(O)_q-$, $(R^{19})(R^{20})NS(O)_q-$, $R^{18}OS(O)_q-$, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $R^{18}OC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–, $R^{18}OS(O)_qO$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, O=, $(R^{19})(R^{20})NN$=, $R^{18}ON$=, $(R^{19})(R^{20})NS(O)_2N$=, NCN=, and O_2NCH=;

or where any pair of R^{13}, R^{14}, R^{15} and R^{16} are optionally joined to form a 5-7 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1 unsaturation, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{18}–, $R^{18}C(O)$–, $(R^{19})(R^{20})NC(O)$–, $R^{18}OC(O)$–, $(R^{19})(R^{20})N$–, $R^{18}C(O)N(R^{21})$–, $(R^{19})(R^{20})NC(O)N(R^{21})$–, $R^{18}OC(O)N(R^{21})$–, N_3–, O_2N–, $R^{18}S(O)_qN(R^{21})$–, $(R^{19})(R^{20})NS(O)_qN(R^{21})$–, $R^{18}O$–, $R^{18}C(O)O$–, $(R^{19})(R^{20})NC(O)O$–, $R^{18}OC(O)O$–, O_2NO–, $R^{18}S(O)_qO$–, $(R^{19})(R^{20})NS(O)_qO$–, $R^{18}OS(O)_qO$–, $R^{18}S(O)_q$–, $(R^{19})(R^{20})NS(O)_q$–, $R^{18}OS(O)_q$–, O=, $(R^{19})(R^{20})NN$=, $R^{18}ON$=, $(R^{19})(R^{20})NS(O)_2N$=, NCN=, and O_2NCH=;

R^{18}, R^{19}, R^{20}, and R^{21} are each independently selected from:

(i) hydrogen;

(ii) C_{1-6}-alkyl, optionally substituted in one or more positions by one or more halogens, H_2N–, MeHN–, EtHN–, *i*-PrHN–, Me_2N–, Et(Me)N–, *i*-Pr(Me)N–, Et_2N–, HO–, MeO–, EtO–, *i*-PrO– or =O;

Q and Q' are substituents connected by a double bond, and are each independently selected from:

O=, S=, R^8N=, $(R^9)(R^{10})NN$=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, O_2NCH=, and $(R^9)(R^{10})C$=;

q is 1 or 2;

as well as pharmaceutically acceptable salts, stereoisomers or prodrugs thereof.

4. A compound according to claim 3 wherein:

X is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) $R^6C(O)N(R^7)$–;

Y is selected from $(R^8)NHC(O)$–, and $R^8OC(O)$–;

Z is a C_{1-8}-alkylene chain or a heteroalkylene chain having 2 to 8 chain atoms, which optionally contains one or more unsaturations, wherein the C_{1-8}-alkylene chain and the heteroalkylene chain may be optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, or O=; and wherein one or more atoms of the C_{1-8}-alkylene chain or the heteroalkylene chain are optionally part of an additional C_{3-8}-cycloalkyl-, or C_{3-8}-heterocycloalkyl-ring, where the said ring optionally contains 1-2 heteroatoms and optionally 1 unsaturation, and optionally is substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, and O=;

R^1 is selected from aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

R^2, R^3, R^4, and R^5 are each independently selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) hydrogen, halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

or any adjacent pair of R^2, R^3, R^4, or R^5 may be part of an alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

provided that at least one of R^2, R^3, R^4, or R^5 is aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

A is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

B is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–,

$R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, and $R^8OS(O)_q$–;

(iv) An alkylene chain having 3 to 4 chain carbon atoms or a heteroalkylene chain having 3 to 4 chain atoms which on each end is connected to adjacent carbons in the aryl or heteroaryl residue, where the alkylene or heteroalkylene chain is optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, R^8O–, and O=;

R^6 and R^7 are each independently selected from:

(i) hydrogen,

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

or where R^6 and R^7 are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1 unsaturation, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_qN(R^{11})$–, $(R^9)(R^{10})NS(O)_qN(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_qO$–, $(R^9)(R^{10})NS(O)_qO$–, $R^8OS(O)_qO$–, $R^8S(O)_q$–, $(R^9)(R^{10})NS(O)_q$–, $R^8OS(O)_q$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

R^8, R^9, R^{10}, and R^{11} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–,

$R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

or where any pair of R^8, R^9, R^{10}, and R^{11} are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1-3 unsaturations, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_qN(R^{16})$–, $(R^{14})(R^{15})NS(O)_qN(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_qO$–, $(R^{14})(R^{15})NS(O)_qO$–, $R^{13}OS(O)_qO$–, $R^{13}S(O)_q$–, $(R^{14})(R^{15})NS(O)_q$–, $R^{13}OS(O)_q$–, O=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

R^{13}, R^{14}, R^{15}, and R^{16} are each independently selected from:

(i) hydrogen;

(ii) C_{1-6}-alkyl, optionally substituted in one or more positions by one or more halogens, H_2N–, MeHN–, EtHN–, *i*-PrHN–, Me_2N–, Et(Me)N–, *i*-Pr(Me)N–, Et_2N–, HO–, MeO–, EtO–, *i*-PrO– or =O;

q is 1 or 2;

as well as pharmaceutically acceptable salts, stereoisomers or prodrugs thereof.

5. A compound according to claim 4 wherein:

X is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) $R^6C(O)N(R^7)$–;

Y is $R^8OC(O)$–;

Z is a C_{1-8}-alkylene chain or a heteroalkylene chain having 2 to 8 chain atoms, which optionally contains one or more unsaturations, wherein the C_{1-8}-alkylene chain and the heteroalkylene chain may be optionally substituted in one or more positions by one or more groups independently selected from halogen, R^8–, $(R^9)(R^{10})N$–, R^8O–, or O=; and wherein one or two carbon atoms of the C_{1-8}-alkylene chain or the heteroalkylene chain may be common to an additional cyclopropyl ring;

R^1 is selected from aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

R^2, R^3, R^4, and R^5 are each independently selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally

substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) hydrogen, halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, and $R^8OS(O)_2$–;

or any adjacent pair of R^2, R^3, R^4, or R^5 may be part of a methylenedioxy, difluoromethylenedioxy, or dimethylmethylenedioxy residue;

provided that at least one of R^2, R^3, R^4, or R^5 is aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from A;

A is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–,

$R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

B is selected from:

(i) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(ii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–,

R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

(iii) halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

R^6 and R^7 are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from B;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

or where R^6 and R^7 are optionally joined to form a 5-6 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1 unsaturation, and which optionally is substituted in one or more positions by one or more

groups independently selected from halogen, NC–, R^8–, $R^8C(O)$–, $(R^9)(R^{10})NC(O)$–, $R^8OC(O)$–, $(R^9)(R^{10})N$–, $R^8C(O)N(R^{11})$–, $(R^9)(R^{10})NC(O)N(R^{11})$–, $R^8OC(O)N(R^{11})$–, N_3–, O_2N–, $R^8S(O)_2N(R^{11})$–, $(R^9)(R^{10})NS(O)_2N(R^{11})$–, R^8O–, $R^8C(O)O$–, $(R^9)(R^{10})NC(O)O$–, $R^8OC(O)O$–, O_2NO–, $R^8S(O)_2O$–, $(R^9)(R^{10})NS(O)_2O$–, $R^8OS(O)_2O$–, $R^8S(O)_2$–, $(R^9)(R^{10})NS(O)_2$–, $R^8OS(O)_2$–, O=, R^8ON=, $(R^9)(R^{10})NS(O)_2N$=, NCN=, and O_2NCH=;

R^8, R^9, R^{10}, and R^{11} are each independently selected from:

(i) hydrogen;

(ii) aryl or heteroaryl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_2N(R^{16})$–, $(R^{14})(R^{15})NS(O)_2N(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_2O$–, $(R^{14})(R^{15})NS(O)_2O$–, $R^{13}OS(O)_2O$–, $R^{13}S(O)_2$–, $(R^{14})(R^{15})NS(O)_2$–, $R^{13}OS(O)_2$–, methylenedioxy, difluoromethylenedioxy, and dimethylmethylenedioxy;

(iii) C_{1-6}-alkyl, C_{3-8}-cycloalkyl, C_{2-6}-alkenyl, C_{2-6}-alkynyl, or C_{3-8}-heterocycloalkyl, wherein any residues herein may be optionally substituted in one or more positions independently of each other by one or more groups selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_2N(R^{16})$–, $(R^{14})(R^{15})NS(O)_2N(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_2O$–, $(R^{14})(R^{15})NS(O)_2O$–, $R^{13}OS(O)_2O$–, $R^{13}S(O)_2$–, $(R^{14})(R^{15})NS(O)_2$–, $R^{13}OS(O)_2$–, O=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

or where any pair of R^8, R^9, R^{10}, and R^{11} are optionally joined to form a 5-8 membered ring, and which ring optionally contains 1-3 heteroatoms and optionally 1 unsaturation, and which optionally is substituted in one or more positions by one or more groups independently selected from halogen, NC–, R^{13}–, $R^{13}C(O)$–, $(R^{14})(R^{15})NC(O)$–, $R^{13}OC(O)$–, $(R^{14})(R^{15})N$–, $R^{13}C(O)N(R^{16})$–, $(R^{14})(R^{15})NC(O)N(R^{16})$–, $R^{13}OC(O)N(R^{16})$–, N_3–, O_2N–, $R^{13}S(O)_2N(R^{16})$–, $(R^{14})(R^{15})NS(O)_2N(R^{16})$–, $R^{13}O$–, $R^{13}C(O)O$–, $(R^{14})(R^{15})NC(O)O$–, $R^{13}OC(O)O$–, O_2NO–, $R^{13}S(O)_2O$–, $(R^{14})(R^{15})NS(O)_2O$–, $R^{13}OS(O)_2O$–, $R^{13}S(O)_2$–, $(R^{14})(R^{15})NS(O)_2$–, $R^{13}OS(O)_2$–, O=, $R^{13}ON$=, $(R^{14})(R^{15})NS(O)_2N$=, NCN=, and O_2NCH=;

R^{13}, R^{14}, R^{15}, and R^{16} are each independently selected from:

(i) hydrogen;

(ii) C_{1-6}-alkyl, optionally substituted in one or more positions by one or more halogens, H_2N–, MeHN–, EtHN–, *i*-PrHN–, Me_2N–, Et(Me)N–, *i*-Pr(Me)N–, Et_2N–, HO–, MeO–, EtO–, *i*-PrO– or =O;

as well as pharmaceutically acceptable salts, stereoisomers or prodrugs thereof.

6. A compound according to any of claims 1-5, which is selected from:

6-(4-*tert*-Butylphenyl)-1-(3-phenoxybenzyl)-3-phenylindole-2-carboxylic acid,
6-(4-*tert*-Butylphenyl)-1-(3-phenoxybenzyl)-3-(2-thienyl)indole-2-carboxylic acid,
5-(3,4-methylenedioxyphenyl)-3-phenyl-1-(3-phenylpropyl)indole-2-carboxylic acid,
3-Phenyl-1-(3-phenylpropyl)-5-(3-pyridinyl)indole-2-carboxylic acid,
6-(4-Benzyloxyphenyl)-3-(3-carboxyphenyl)-1-(3-nitrobenzyl)indole-2-carboxylic acid,

3-(3-Carboxyphenyl)-4-phenyl-1-(3-trifluoromethylbenzyl)indole-2-carboxylic acid,
6-(4-Benzyloxyphenyl)-1-(3-nitrobenzyl)-3-(2-oxopyrrolidin-1-yl)indole-2-carboxylic acid,
3-(2-Oxopyrrolidin-1-yl)-1-(3-phenoxybenzyl)-5-phenylindole-2-carboxylic acid,
1-(3,5-Difluorobenzyl)-4-methoxy-3-(2-oxopyrrolidin-1-yl)-7-phenylindole-2-carboxylic acid,
6-(3,4-Methylenedioxyphenyl)-1-(3,5-bis-trifluoromethylbenzyl)-3-(4-chlorobenzoylamino)indole-2-carboxylic acid,
3-(3,5-Dimethoxybenzoylamino)-5-(4-nitrophenyl)-1-(3-phenoxybenzyl)indole-2-carboxylic acid,
3-(3-Amino-4-methylbenzoylamino)-5-(4-*tert*-butylphenyl)-1-(3-chlorobenzyl)indole-2-carboxylic acid,
5-(4-*tert*-Butylphenyl)-1-(3-chlorobenzyl)-3-[(pyridine-3-carbonyl)-amino]-indole-2-carboxylic acid,
3-(4-dimethylaminobutyrylamino)-6-(3,4-methylenedioxyphenyl)-1-(3-phenoxybenzyl)indole-2-carboxylic acid,
1-(3-Cyanobenzyl)-6-(3,4-methylenedioxyphenyl)-3-(3-phenylacryloylamino)indole-2-carboxylic acid,
1-(3-Carbamoylbenzyl)-6-(3,4-methylenedioxyphenyl)-3-(3-phenylacryloylamino)indole-2-carboxylic acid,
3-Acetylamino-5-(3,4-methylenedioxyphenyl)-1-(5-phenoxypentyl)indole-2-carboxylic acid,
5-(3,4-Methylenedioxyphenyl)-3-(2-oxopiperidin-1-yl)-1-(5-phenoxypentyl)-indole-2-carboxylic acid,

as well as pharmaceutically acceptable salts, stereoisomers or prodrugs thereof.

7. A compound according to any of claims 1-6 for use as a pharmaceutical.

8. A pharmaceutical composition comprising therapeutically effective amounts of a compound according to any of claims 1-6 together with a pharmaceutically acceptable diluent or carrier.

9. Use of a therapeutically effective amount of a compound according to any of claims 1-6 for the preparation of a pharmaceutical composition for alleviating, preventing, inhibiting, or treating a disease, disorder, or condition associated with inflammation, pain, or fever by administering to a subject in need of treatment thereof.

10. Use of a compound according to any of claims 1-6 by combining it with one or more compounds that are useful for alleviating, preventing, inhibiting, or treating a disease, disorder, or medical condition associated with inflammation, pain, or fever by administering to a subject in need of treatment thereof.

11. A process for preparation of the pharmaceutical composition according to claim 8 by combining a compound according to any of claims 1-6 together with a pharmaceutical diluent or carrier.

12. A method for alleviating, preventing, inhibiting or treating a disease, disorder, or condition associated with inflammation, acute or chronic pain, or fever, such as: inflammatory bowel disease, irritable bowel syndrome, migraine, headache, low back pain, fibromyalgia, myofascial disorders, viral infections (*e.g.* influenza, common cold, herpes zoster, and AIDS), bacterial infections, fungal infections, dysmenorrhea, burns, surgical or dental procedures, malignancies (*e.g.* breast cancer, colon cancer, and prostate cancer), atherosclerosis, gout, arthritis, osteoarthritis, juvenile arthritis, rheumatoid arthritis, rheumatic fever, ankylosing spondylitis, systemic lupus erythematosus, vasculitis, pancreatitis, nephritis, bursitis, conjunctivitis, iritis, scleritis, uveitis, wound healing, dermatitis, eczema, psoriasis, stroke, diabetes mellitus; neurodegenerative disorders such as Alzheimers disease and multiple sclerosis, autoimmune diseases, osteoporosis, asthma, chronic obstructive

pulmonary disease, pulmonary fibrosis, allergic disorders, and rhinitis, by administering to a subject in need of treatment thereof a therapeutically effective amount of a compound according to any of claims 1-6.

13. A method for eliciting a modulating effect on the membrane associated prostaglandin E_2 synthase (mPGES) enzyme in a subject in need of treatment, which comprises administering to the subject of a therapeutically effective amount of a compound according to any of claims 1-6.

ABSTRACT

This invention relates to novel compounds, to pharmaceutical compositions comprising the compounds, as well as to the use of the compounds in medicine and for the preparation of a medicament, which acts on the membrane associated prostaglandin E_2 synthase (mPGES) enzyme. It is of special interest to provide a treatment or alleviation of inflammatory diseases and disorders having an inflammatory component, for the treatment or alleviation of pain, and for the alleviation of fever.

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☑ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.